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The prevalence & correlates of first episode psychosis (FEP) and the impact of trauma and discrimination on risk of FEP

Onyejiaka, Adanna Nkeiru

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VOLUME I

SYSTEMATIC LITERATURE REVIEW AND MAIN RESEARCH PROJECT

ADANNA ONYEJAKA

INSTITUTE OF PSYCHIATRY, PSYCHOLOGY AND NEUROSCIENCE

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Systematic Review

Psychosis, trauma and ethnicity: Are there ethnic variations in the rates of comorbid trauma/PTSD and psychosis? A systematic review of the literature

Adanna Onyejiaka

Supervised by Professor Craig Morgan & Dr Lucia Valmaggia

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Systematic Review

Psychosis, trauma and ethnicity: Are there ethnic variations in the rates of comorbid trauma/PTSD and psychosis? A systematic review of the literature.

1. Abstract

Background. Exposure to trauma has been linked with the onset and maintenance of psychosis.

As trauma is a prerequisite for Post-Traumatic Stress Disorder (PTSD), it also raises the question of potential associations between the two psychiatric disorders. The prevalence rates for PTSD symptoms in psychosis is estimated at 40% and between 20-40% for the inverse relationship. Furthermore, research data have evidenced ethnic differences in the rates of psychosis and PTSD, as well as experience of trauma, independently. However, research investigating the coexistence of this phenomenon and ethnic variations in the prevalence rates is limited. Thus, this review sought identify, critically evaluate the literature and summarise the prevalence of comorbid trauma/PTSD and psychosis, looking at whether rates of these vary by ethnicity.

Method. PsycINFO, MEDLINE and Web of Science electronic databases were searched for studies reporting the comorbidity rates of trauma/PTSD and psychosis disaggregated by ethnic groups. Findings were synthesised qualitatively for eligible studies relevant to the review question. In addition, a quality assessment of included studies was conducted with the aim of determining the methodological rigour and robustness of conclusions that can be reached.

Results. A total of 751 citations were screened and nine studies (sample size between studies varying from 18 to 8124 participants) were identified as meeting inclusion criteria for this review. Five studies showed evidence of ethnic variations in comorbid prevalence rates of trauma/PTSD and psychosis. However, there were variations between studies in the methodology used with some limitations identified, resulting in varying quality of the literature.

Conclusion. Although some findings supported the disaggregation of experiences studied by ethnicity, it is not possible to draw firm conclusions given the heterogeneity and limitations of methodology identified. Future research direction should aim for quantitative synthesis and addressing methodological practices.

2. Introduction/ Literature review

2.1 Lifetime Trauma and PTSD

Definitions of trauma have varied over the years. It is a term which has been reinvented and changed particularly in line with the advent of new diagnostic manuals. The original definition of trauma in the DSM-III and DSM-III-R was described as events occurring outside the normal range of human experience (American Psychiatric Association, 1980, 1987). However, the definition of trauma has since evolved and redefined in subjective terms with emphasis on individual differences on how people may perceive or respond to similar events (Breslau, 2002). Traumatic events are characterised as situations or experiences that are emotionally distressing and usually involve an element of perceived threat, broadly defined (Breslau, 2002). Lifetime trauma refers to significantly distressing events (including but not limited to experiences of interpersonal violence; sexual/ physical/emotional abuse; neglect; natural disaster; military combat; mass violence; life threatening accident) which may occur for an individual at any point in their life, whether during childhood or as an adult. The event could be single, discrete incidents or a series of cumulative and persistent exposure to severe events over the life course (Ehlers & Clark, 2000; NICE, 2005; Terr, 1991). Traumatic experiences are considered to be common in the general population (Ehring, Ehlers, & Glucksman, 2008), however, there may be variation in severity, duration, type and individual differences in reactions to these events (for review, see Brewin, Andrews, & Valentine, 2000).

Post-Traumatic Stress Disorder (PTSD) is one of the many possible reactions which could develop following exposure to a traumatic event. PTSD is a mental health disorder and refers to a pattern of symptoms which are observed following the experience of trauma (e.g. when an individual witnesses or is exposed to life threatening event). These symptoms patterns are often impairing and distressing for the individual and fall under four core clusters: a) re-experiencing of traumatic experiences; b) increased arousal or reactivity/ marked anxiety; c) dissociation and effortful avoidance of associated reminders or trauma memory; and d) negative alterations in

beliefs and emotions following confrontation with a traumatic event (e.g. experienced or witnessed) in which the individual perceived an actual or threatened death or serious injury, or threat of physical integrity of self or others (DSM-V; American Psychiatric Association, 2013). To meet diagnostic criteria in the DSM-V, the symptoms are required to last at least one month and cause significant impairments in adaptive and social functioning. The ICD-10 (World Health Organization, 1992), places more emphasis on the re-experiencing aspects of the event or stressor which may reoccur in the form of nightmares, flashbacks or intrusive memories.

Exposure to traumatic events and PTSD have been significantly researched in the last few years (Maercker et al., 2013; Mauritz, Goossens, Draijer, & van Achterberg, 2013). Whilst trauma has been implicated in the onset, relapse and outcomes of a range of psychiatric disorders, PTSD is unique in including exposure to trauma as an aetiological criterion essential for diagnosis (Scott & Stradling, 1994).

Prevalence rates of PTSD have increased in the last few decades, perhaps reflecting diagnostic changes (particularly between the DSM-III to DSM-IV-TR) or greater awareness and recognition of the disorder amongst clinicians (Norris & Slone, 2007). In the UK, a survey conducted by McManus and colleagues (2009) estimated the prevalence of PTSD to be 3%. Prevalence rates for PTSD in other countries have ranged from approximately 0% – 8% (see review; McManus et al., 2009). However, the reason for variation of prevalence is not clear and may be accounted for by different methodological approaches. Nevertheless, the rates of PTSD and relationship with trauma is unclear, not least due to reports that lifetime prevalence rates for trauma in the general population have been estimated as high as 90% in some studies (for reviews, see; Atwoli, Stein, Koenen, & McLaughlin, 2015; Breslau, 2009; de Vries & Olf, 2009; Dorrington et al., 2014; McManus et al., 2009). This highlights an important issue to note, that only a small minority of people will go on to develop PTSD following exposure to trauma (McManus et al., 2009). As noted above, there are individual differences as the experience of

trauma can be subjective, which can be influenced by many different factors (e.g. perceived level of threat, quality of recovery environment, personal development history). Therefore, how an individual makes sense of their experience may vary in different contexts and over the course of time. There may also be variations in relation to the nature and severity of the traumatic event (Ehlers & Clark, 2000), as well as a range of reactions and other disorders which could develop following trauma incidents (Resick, 2001). Overall, stress reactions can occur whether the events are objective or subjective (Carter, 2007). Reactions will vary on many dimensions such as intensity, frequency, duration and level of impairment which will differentiate between acute non-pathological responses from mental illness. In addition, comorbidity rates of PTSD with other common psychological disorders have been estimated as high as 80% (Foa, Keane, & Friedman, 2000) with variations reported for sociodemographic factors such as gender (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). Needless to say, exposure to trauma lacks specificity and could lead to wide range of outcomes.

2.2 Psychosis

Exposure to trauma have also been implicated in the aetiology of psychosis. Psychosis is the umbrella term in which disorders such as schizophrenia, schizoaffective, schizophreniform, schizotypal and delusional disorders fall under (American Psychiatric Association, 2013; NICE, 2014; World Health Organization, 1992). Psychosis represents a severe mental illness (SMI) characterised by significant distortions in an individual's perception, thoughts, mood and behaviour. Symptoms are usually divided into so called 'positive symptoms', which include hallucinations (unusual experiences in any sensory modality in the absence of any stimulus), delusions (holding a fixed or falsely held beliefs), and 'negative symptoms' (such as lack of emotional reactivity, anhedonia, poverty of speech, social isolation or detachment and self-neglect) (American Psychiatric Association, 2013; NICE, 2014; World Health Organization, 1992). However, the disorders which fall under this diagnostic concept are considered to be

heterogeneous as the conditions notably vary in the nature, symptom severity and duration, degree of impairment and level of distress caused even within the same diagnostic categories. For instance, there remains an infinite range of ways in which the presentation of those diagnosed with schizophrenia can differ between individuals.

General population estimates of the prevalence of psychosis have been examined. Van Os and colleagues (2009) reported an estimated lifetime prevalence of psychosis as approximately 3.5%. The prevalence rates for schizophrenia specifically are lower with an estimated risk around 0.4% to 2.3% (for reviews, see; Saha, Chant, Welham, & McGrath, 2005; Van Os & Kapur, 2009), with variations in estimates by demographic factors. Onset is typically in early adulthood between the ages of 16 to 30 years (Mueser & McGurk, 2004). In a meta-analysis review, Kirkbride and colleagues (2012) found a pooled incidence rate for all psychotic disorders was approximately 32 per 100,000 per year, and at 15 per 100,000 per year for schizophrenia (in England between 1950 – 2006). However, as with prevalence rates, estimates vary depending on the country of study, geographic location e.g. urban vs rural setting, sociodemographic information considered e.g. ethnic group, gender and socioeconomic status and methodology utilised (see; Fearon et al., 2006; Kirkbride et al., 2006; J. McGrath et al., 2004; J. J. McGrath, 2006; Perälä et al., 2007; Van Os & McGuffin, 2003). In addition, psychiatric comorbidity of psychosis with other disorders are high and involve a range of common mental health conditions such as depression and anxiety, including PTSD (Buckley, Miller, Lehrer, & Castle, 2009; Freeman & Garety, 2003; Seow et al., 2016; Upthegrove et al., 2010; S. Young et al., 2013).

Psychotic disorders are considered to be generally influenced by a combination of multiple genetic and environmental aspects, with many interconnected risk and maintenance factors. The conventional view that biological or genetic factors are solely implicated in onset and maintenance of schizophrenia and other psychoses have been critically reviewed and shifted somewhat in the last few decades with studies focusing on the potential influences of key

psychological and social factors in the aetiology of psychosis (Zubin & Spring, 1977). The experience of trauma has been one such factor which has been investigated both in relation to the development and maintenance of psychotic disorders.

2.3 Trauma, PTSD and Psychosis

The role of trauma and their associated consequences have been implicated with the onset and persistence of psychosis due the number of individuals presenting with a history of traumatic experiences (for reviews, see; Bendall, Jackson, Hulbert, & McGorry, 2008; Cutajar et al., 2010; Fisher et al., 2010; Manning & Stickley, 2009; Read, Os, Morrison, & Ross, 2005). This association can be explicated with reference to the stress-diathesis vulnerability theory (e.g. Nuechterlein & Dawson, 1984; Zubin & Spring, 1977) which proposes that mental health disorders manifest from the interaction between predispositional stress vulnerability, experience of stressors (e.g. at individual level and/or interpersonal) and the individual's ability to cope. Other models have expanded on this by highlighting how these factors interact to affect outcomes (see; Docherty, St-Hilaire, Aakre, & Seghers, 2009; Liberman et al., 1986; Yanos & Moos, 2007). The course and outcomes of response are generally thought to be influenced by the regulation of stress with coping resources playing an important role in this view (Rudnick & Martins, 2009). In relation to psychosis, the experience of trauma could be considered a stressful life event, as well as a potential stressor which predisposes individuals to vulnerability or increased sensitivity (Morrison, 2009). As a result of pre-existing factors and circumstances, individuals are likely to differ in the way they cope with threatening events (Dohrenwend, 2000). It is thought that social factors (individual, interpersonal, societal) can change or interact with the expression of biological risk factors (Shah, Mizrahi, & McKenzie, 2011). Thus, vulnerability could be conceived of as the combined influence of biopsychosocial, as well as epigenetic processes that in turn result in heightened 'sensitisation' to environmental stressors which in some individuals may lead to the formation and maintenance of psychotic symptoms (Collip, Myin-Germeys, & Van Os, 2008;

Kirkbride & Jones, 2010; March & Susser, 2006). This proposed developmental synthesis are in line with the traumagenic neurodevelopment model of psychosis (for review, see; John Read, Fosse, Moskowitz, & Perry, 2014).

Whilst trauma can occur across the lifespan in different contexts, in relation to the aetiology of psychosis, childhood trauma has been the focus of attention, demonstrating a strong association with psychotic symptomology (Larkin & Read, 2008; Manning & Stickley, 2009; Morgan & Fisher, 2007; Read et al., 2005; Whitfield, Dube, Felitti, & Anda, 2005). In addition, some studies have demonstrated an association between childhood trauma and specific psychotic symptoms (across the continuum of expression) in both clinical and non-clinical populations (e.g. Ashcroft, Kingdon, & Chadwick, 2012; Bentall, Wickham, Shevlin, & Varese, 2012; Heins et al., 2011; Morrison & Petersen, 2003) as well as in people at ultra-high risk (Judy L Thompson et al., 2009). For example, Morrison and Petersen demonstrated an association between trauma and predisposition to auditory hallucinations in the general population. Recent meta-analyses by Varese and colleagues (2012) and Matheson and colleagues (2013) found childhood trauma increased the risk of psychosis in adulthood with an odds ratio (OR) of 2.8 and 3.6 respectively. Some studies have expanded on this finding, demonstrating a dose-response relationship as frequent and more severe forms of childhood trauma elevate the risk of psychosis later on (Kelleher et al., 2013; Larkin & Read, 2008; Schäfer & Fisher, 2011; Whitfield et al., 2005).

Furthermore, in considering the potential role of trauma in psychosis, it is also necessary to consider the potential overlap with PTSD. The experience of trauma is an essential prerequisite for the diagnosis of PTSD. The experience of trauma, therefore, may be the common criterion for the onset and development of PTSD and psychosis as it is implicated in both disorders (Powers, Fani, Cross, Ressler, & Bradley, 2016). Some models have highlighted common developmental and maintenance factors which can be applied to both PTSD and

psychosis (Morrison, Frame, & Larkin, 2003). Thus, there may be obvious overlapping features of developing a psychotic disorder and a PTSD diagnosis. This is supported by phenomenological similarities between psychotic and PTSD symptoms. For example, symptoms of avoidance and emotional numbing in PTSD have been argued to mirror negative symptoms such as anhedonia and avolition in psychosis (Stampfer, 1990). Other research have suggested that trauma-induced dissociative responses were associated with positive psychotic symptoms (Kilcommons & Morrison, 2005; Vogel et al., 2009). In fact, significant overlap in experiences of dissociative and psychotic symptoms have been demonstrated (Allen, Coyne, & Console, 1997; Longden, Madill, & Waterman, 2012).

In addition, it is well documented the PTSD is common among those with psychosis (with some studies suggesting a prevalence of around 40%; Mueser et al., 1998) and, vice versa, that psychotic symptoms are more common in PTSD (with reports between 20 and 40%; Seedat, Stein, Oosthuizen, Emsley, & Stein, 2003). In a recent meta-analysis by Achim and colleagues (2011), prevalence rates of PTSD in individuals with psychosis as high as 51% were identified. While these studies have confirmed basic relationships between trauma, PTSD and psychosis, research have also shown evidence of specificity, i.e. that PTSD is associated with specific psychotic symptoms and poorer outcomes. For example, some studies have shown that comorbid PTSD confers with greater severity of delusions and hallucinations and heightened paranoia (Gracie et al., 2007; Sautter et al., 1999), impaired functioning (Calhoun, Bosworth, Stechuchak, Strauss, & Butterfield, 2006; Lysaker, Meyer, Evans, Clements, & Marks, 2001) and increased risk of suicide (Strauss et al., 2006). These observations provide fundamental reasons for investigating the relationship between trauma, PTSD and psychosis further.

2.4 The importance of ethnicity

There has been an increasing evidence-base highlighting the importance of considering ethnicity in psychosis research given the disproportionate rates of psychotic disorders in minority ethnic groups compared to ethnic majority (Fearon & Morgan, 2006; Harrison, 1990; Harrison, Owens, Holton, Neilson, & Boot, 1988; Kirkbride, Errazuriz, et al., 2012; Morgan et al., 2006; Sharpley, Hutchinson, Murray, & McKenzie, 2001). The AESOP (Aetiology and Ethnicity in Schizophrenia and Other Psychoses) demonstrated approximately seven-fold and four-fold increase of psychosis in the Black Caribbean and Black African samples, respectively, compared to the White British group (Morgan et al., 2006). A large-scale community sample found that non-white ethnicity was associated with increased probability of experiencing auditory hallucinations (Shevlin et al., 2011). The evidence-base for ethnic difference within psychosis have not only been demonstrated in clinical presentations. There are also data to suggest that ethnic minority groups experience poorer social, clinical and service use outcomes than their White counterparts (Bhui et al., 2003; Morgan et al., 2017; Morgan et al., 2005; Morgan, Mallett, Hutchinson, & Leff, 2004; Sharpley et al., 2001). Contemporary research in this area have highlighted socioenvironmental adversity, broadly defined, and migration as the possible contributing factors for these phenomena (e.g. Cantor-Graae & Selten, 2005; Kirkbride et al., 2007; Morgan et al., 2009; Morgan et al., 2008; Reininghaus et al., 2010). There is less consensus in relation to which key explanatory processes are involved and the associations remain poorly understood. Social adversity, broadly defined, may account for the elevated rates in minority ethnic groups (e.g. Cooper, 2005; Karlsen & Nazroo, 2002; Mallett, Leff, Bhugra, Pang, & Zhao, 2002; McKenzie, Fearon, & Hutchinson, 2008; Morgan et al., 2008; Morgan et al., 2005; Sharpley et al., 2001). However, the explanations are complicated by the fact that ethnic status can be an antecedent source of disadvantage (Dohrenwend, 2000). For example, Modood and colleagues (1997) found that non-white groups in the UK, particular of African or Caribbean origin, were significantly more likely to experience social adversity (e.g. unemployment, poor housing). In

addition, it is difficult to distinguish the independent contributory influence of ethnicity and migration on social contexts and experiences as these factors are interlinked (McKenzie et al., 2008). These complexities have been illustrated in Cantor-Graae and Selton's (2005) meta-analysis. They found that although the risk of schizophrenia was elevated in all migrant groups, the associations were strongest for those migrating from areas where there was a black majority population, and were migrating from developing to developed countries. Moreover, the second-generation migrants were at even greater risk than first generation migrants. Therefore, in considering ethnicity, it is also important to think about the influence of migration. Research in this area shows that migration may be of key importance, particularly because migrants do not typically come from places with high rates of psychosis (e.g. Bhugra et al., 1996; Mahy, Mallett, Leff, & Bhugra, 1999). Thus, the explanation for the elevated rates of psychosis may lie in the post-migration factors, for example, adverse social environments related to ethnic status (Bourque, van der Ven, & Malla, 2011). Nonetheless, separating ethnicity from migration can be difficult (Bresnahan et al., 2007).

As highlighted above, specific types of trauma have been linked with certain types of psychotic symptoms. Ethnic specific differences have also been found in this relationship. For example, some evidence suggests that hallucinations are more frequently reported in minority ethnic groups such as Afro-Caribbeans in the UK and African-Americans and Latinos in the USA (Harvey, Williams, McGuffin, & Toone, 1990; Strakowski, McElroy, Keck, & West, 1996). An interesting finding, given that emotional and sexual trauma in particular, have been associated with auditory verbal hallucinations in clinical and non-clinical populations (Bentall et al., 2012; Daalman et al., 2012).

The prevalence rates for trauma and PTSD have also been shown to vary by ethnicity. In relation to trauma research, the prevalence rates of childhood abuse in minority ethnic groups is often under-recognised (Berg et al., 2015). However, in children services the number of ethnic

minorities tend to be disproportionately higher and are more likely to be placed in foster care than majority ethnic groups (e.g. Hill, 2007). Thompson and colleagues (2009) found that childhood abuse was significantly associated with severity of attenuated positive symptoms, and additionally that this was accounted for by greater trauma exposure in ethnic minority individuals at high risk of psychosis. The same was found in individuals with prodromal symptoms of psychosis which demonstrated that ethnic minorities were exposed to more childhood trauma (Wigman et al., 2011).

Studies investigating the epidemiological patterns of PTSD have found important differences according to ethnicity, although the evidence-base is inconclusive. A meta-analysis by Brewin and colleagues (2000) found that ethnic minority status was associated with elevated rates of PTSD. Other studies have found that ethnic minority groups have elevated levels of stress which is not fully explained by the experience of traumatic events. For example, one study showed that despite the experience of trauma being more elevated in the White sample, when considering the impact of trauma, Black men were especially vulnerable to exhibiting the highest levels of stress following a traumatic event (Norris, 1992). Other studies have revealed contradictory evidence and highlighted the complexity of the effects of trauma on health outcomes in relation to ethnicity. One such study showed that although the Black sample were initially less traumatised (Gleser, Green, & Winget, 2013), a disproportionate number later exhibited delayed-onset PTSD (Green et al., 1990). However, whilst some studies have shown ethnic differences in individuals presenting with PTSD, others have shown no such difference (see; Frueh et al., 2002; Frueh, Brady, & de Arellano, 1998; Frueh, Gold, deArellano, & Brady, 1997; Monnier, Elhai, Frueh, Sauvageot, & Magruder, 2002; Trent Jr, Rushlau, Munley, Bloem, & Driesenga, 2000). Another interesting finding in relation to effects of ethnicity, is that one study found that the strength of an individual's ethnic identity was protective and seemed to

buffer effects of stress related to racial/ethnic discrimination (Mossakowski, 2003). Thus, strong ethnic identity was a potential coping resource which prevented negative health outcomes.

2.5 Rationale for review

As discussed above, reports have shown ethnic variations in both psychosis and PTSD populations as well as in the experiences of trauma. The experience of trauma/PTSD and psychosis can be highly debilitating. The burden of trauma/PTSD (Jacobsen, Southwick, & Kosten, 2001; Kessler, 2000) and psychosis (Collins et al., 2011; Murray, 2012; NICE, 2014), independently, are considerable both in morbidity and mortality, in association with a high risk factor for suicide and their contribution to dislocations in adaptive social and occupational functioning. They can be universally impairing for individuals, families, communities, society, healthcare services and economy (Knapp, Mangalore, & Simon, 2004; Van Os & Kapur, 2009). In addition, studies have documented the burden comorbidity of these experiences can create in clinical and social outcomes.

In the brief review of the literature, a number of limitations have been highlighted. Whilst the majority of studies have investigated the relationship between childhood trauma, PTSD and psychosis, the contribution of lifetime, in particular traumatic experiences as an adult are often not considered in the literature (especially in psychosis studies). Some prospective studies in this area potentially highlight the importance of considering lifetime trauma as they have demonstrated a dose-response effect which suggests that exposure to early trauma may predispose individuals to later experiences of trauma and thus increases risk of psychosis proneness (Spauwen, Krabbendam, Lieb, Wittchen, & Van Os, 2006). Although, the research base has yielded equivocal findings. In addition, much of the epidemiological evidence surrounding comorbidity comes from studies of veterans and there remains a dearth in the research base investigating the relationship between lifetime trauma/PTSD, psychosis and ethnicity. As a result, information regarding the prevalence, characteristics of and outcomes for

these groups remain sparse and this may have implications for policy and practice in mental health and general population.

Prevalence rates have been shown to vary which can be a function of numerous factors including methodological issues as well as the differences in the conceptualisations of mental health presentations, demographic factors considered and types of experiences investigated within the literature. A review of comorbid rates in these experiences in the first instance is pertinent given the inconsistent findings. Therefore, a systematic review, investigating the prevalence rates of comorbidity, whilst taking account of the methodology seems timely.

Given the research highlighting ethnic differences in presentation, ethnicity seems like an important factor to consider. Ethnicity being a stable, albeit a difficult concept to operationalise reliably and validly given its interconnectivity with race, culture and migration, lends itself to this kind of investigation. However, often in research, the role of ethnicity is often overlooked or not measured consistently. Although the effects of trauma are acknowledged and researched in relation to mental health, the variation and differences between ethnic groups tend to be less studied.

The highlighted issues above make for compelling reasons to examine the prevalence of comorbid experiences of trauma/PTSD, psychosis and the role of ethnicity. Whilst various attributes may place an individual at increased odds of experiencing trauma and/or developing PTSD or psychotic disorder, the combined impact of both disorders on different groups has not been fully investigated. Ethnicity could be one such attribute which merits further investigation as it is implicated in differing prevalence rates of trauma and/or PTSD and in psychosis.

2.6 Objectives of review

This systematic review aims to evaluate the existing literature and report on the prevalence comorbid experience of trauma/PTSD and psychosis, exploring whether there is any evidence of variations by ethnicity. Studies that failed to document or specify the presence of comorbid prevalence of psychosis and trauma and/or PTSD within different ethnic populations were therefore not included. The study objectives are:

- (i) To review all published, original studies reporting the prevalence of co-occurring trauma/PTSD and psychosis within defined ethnic group populations.
- (ii) To highlight additional evidence, if available, on the possible hypotheses and mechanism if such variations by ethnicity exists.

3. Method

3.1 Eligibility criteria

3.1.1 Inclusion criteria

Studies were included if:

- they assessed trauma and or PTSD;
- they assessed psychosis or psychotic symptoms;
- they statistically and explicitly reported the prevalence of co-occurring trauma and/or PTSD and psychosis by ethnic groups;
- individuals in the sample were ages 18-65 (similar to age group of participants in main research project);
- they were published in English in peer review journals;
- studied human participants; and
- adopted a quantitative study design that incorporated all the above.

All searches were limited to journal articles from the inception date of each database till the 17th January 2017 when the final searches were completed.

The age groups of adults included also reflect the organisation of services in the UK, thus to make studies comparable only those which recruited adults aged between 18 and 65 were included. Studies looking at single ethnic groups were include for the purpose of looking at prevalence rates within these groups.

Studies were included if they assessed symptoms or experiences using standardised measures, whether objective or subjective measure, including self-report questionnaire. There was no specification on the type of measure, but studies were required to use validated measures. Prospective and retrospective studies were included. To be as inclusive as possible, studies which investigated comorbid trauma/PTSD and psychosis within the context of other psychiatric disorders were included as long as the analyses were disaggregated by ethnicity. This information was usually determined during the review of the full text of the article.

3.1.1.1 Parameters for concept 1: Psychosis/psychotic symptomology

In the current study, the concept of psychosis was defined by diagnosis of schizophrenia spectrum disorder or psychotic disorder made by clinicians or researchers in line with diagnostic manuals at the time of the study or clinical judgement (see Appendix 8.1 for further details).

3.1.1.2 Parameters for concept 2: Trauma/PTSD

Trauma was defined as significantly distressing events (irrespective of frequency, duration and type of trauma experienced, severity) which occurred at any point during the life course of samples studied (measured objectively or subjectively i.e. self-report). These experiences were not necessarily required to result in a diagnosis of PTSD, thus, any study reporting that the

sample had experienced trauma was included. The term for trauma was expanded in the review so as to not omit any relevant literature. However, studies looking at acquired or traumatic brain injury or medically related trauma without reference to trauma experiences were excluded. Further details for the parameters of this concept are included in Appendix 8.2.

3.1.1.3 Parameters for concept 3: Ethnicity

Ethnicity and ethnic groupings remain highly disputed concepts, although ethnicity has been extensively studied in sociological and anthropological fields (Brown & Langer, 2010; Stronks, Kulu-Glasgow, & Agyemang, 2009). Despite the lack of ubiquitous definition, the general notion is that ethnicity refers to a common sense of identity to a group who share collective history, values, culture, geographical location and language (Aspinall, 2001; Berthoud, 1998; Senior & Bhopal, 1994; Singh, 1997). In addition, there are a vast number of ways to operationalise ethnicity, including country of birth of the individual or their parents as an indicator (Stronks et al., 2009). This highlights the difficulty in operationalising ethnicity as it can be subjectively interpreted and have several and ambiguous meanings, often overlapping with political notions of nationality and migration status (Singh, 1997). There is also an inherent link or overlap between race and culture with ethnicity. Thus, for the purpose of this review, ethnicity was defined as broadly as possible in line with the researchers' definitions (e.g. whether based on country of origin or attained through self-report) to encapsulate and cover the topic area with as much breadth as possible. This was thought to be the best approach as there is no universally accepted definition of ethnicity, the concept is often conceptualised inconsistently and differences in conceptualisation may be encountered cross-culturally (Brown & Langer, 2010). In addition, Brown and Langer (2010) argue that despite the varying methodologies utilised to define ethnicity that as long as the interpretation of findings acknowledges these limitations, quantitative analysis can provide a useful and systematic form of comparison. This was additionally addressed in the review by including a quality measurement for categorisation of

ethnicity. This review is concerned with the concept of ethnicity and its relationship to comorbid trauma/PTSD and psychosis.

Given the likelihood that refugee samples may represent individuals from ethnic minority groups, studies investigating these populations were included if they met all the relevant criteria for the review. Refugee groups are also less likely to access clinical settings, thus no restriction in relation to context or settings for presentation were applied. The review, therefore, included clinical as well as non-clinical samples.

As the review was interested in prevalence of the comorbidity (relevant to topic) by ethnicity, there was no requirement for studies to have a comparison or control group. Thus, studies only looking at one ethnic group in particular were included. Studies which did not report disaggregated data by ethnic groups for comorbidity of trauma/PTSD and psychosis, however, were not included.

3.1.2 Exclusion criteria

Studies were excluded if they met the following criteria:

- assessed life events only and not trauma specifically or did not statistically differentiate between life events and trauma;
- assessed psychotic-like experiences;
- studies which did not report or distinguish differences in the prevalence of co-occurring experiences of trauma/PTSD and psychosis by ethnic group;
- included participants aged under 18 or over 65 where these individuals were included in analyses without any distinction by age i.e. no clear clarification or reporting that separated the analyses from those aged 18-65 (due to reasons stated above);

- studies with sample size less than five for any of the required concepts;
- qualitative analyses or systematic reviews;
- grey literature (including unpublished studies/not peer reviewed, theses, abstracts, book chapters) or case studies $n < 5$; and
- not published in English or non-human sample.

It was beyond the scope and feasibility of this review to contact authors directly, thus, if there were key information required that were not reported or unclear in the paper, these were excluded from the review. Thus, ultimate inclusion of the studies was dependent on their contribution to fulfilling the main research question and meeting the research objectives, while meeting the defined inclusion criteria.

3.2 Study selection

3.2.1 Information sources and search strategy

A comprehensive and systematic search of the relevant literature was conducted on electronic databases using predefined search terms. The search strategy was applied using the PsycINFO, MEDLINE and Web of Science (WoS) databases (with searches conducted independently in each database). The searches were conducted to identify all relevant literature published from the inception of the database till the 17th of January 2017. Search terms were clustered into three concepts: a) psychosis; b) trauma/PTSD; and c) ethnicity. Search terms within the same concept were conducted independently and then combined with the Boolean 'OR' operator; and then combined with the 'AND' between concepts, for example ([all search terms concept 1 combined with OR] AND [all search terms concept 2 combined with OR] AND [all search terms concept 3 combined with OR]) – see Table 3 in Appendix 8.3 for further details.

3.2.2 Data collection and extraction

All records identified using the search strategy from all the database were first combined onto Endnotes (Version 7.7.1; Thomson Reuters) reference manager programme. After the search results from all three databases were combined, duplicate papers were removed after which all remaining papers were screened for relevance against the inclusion and exclusion criteria. Initial screening for eligibility and relevance was performed by the primary researcher, based on information in the titles and abstracts. Full text versions of papers which were not excluded from the initial criteria were obtained (with the exception of one paper which full text version could not be obtained) and screened by primary researcher before the final papers for inclusion were selected. Studies without abstracts but with titles suggesting that they were relevant to the objectives of this review were also selected for full-text screening. Full text were retrieved either through Endnotes, Google scholar or 'Research Gate'. Reasons for exclusion were only registered for full text screening – see Table 4 in Appendix 8.3 for further details. Corresponding authors of the studies were not contacted to gather additional information (in cases where information relevant to the review was incomplete, inaccurate, unclear or missing data) or full text version due to time restrictions. Five papers from the final included papers were randomly selected using a random number generator (www.random.org) to be screened by a second reviewer using the quality assessment tool to ensure that information extracted were consistent. For articles in which there was disagreement between the two reviewers, these were resolved by discussion before making a decision regarding inclusion and/or quality rating. A data extraction form was created for the purposes of this review in order to code the data (see Appendix 8.4 for details of information extracted).

3.3 Quality assessment

The 'Quality Assessment Tool for Observational Cohort and Cross-sectional Studies' (US Department of Health, 2015; see Appendix 8.6 and 8.7 for criteria items and guidance for

assessment of quality) was used to assess the quality of each eligible study in the review. This quality measure used to assess risk of bias and the questions for each criteria are used as a guide to evaluate the internal validity of a study (see Appendix 8.7 for more information on how bias was assessed).

3.4 Data synthesis

Outcomes were subject to narrative synthesis with interpretation of evidence from the included studies, related to the review question. Outcomes analysed in the qualitative analyses were:

- (i) methodology design (e.g. cross-sectional, case-series)
- (ii) Recruitment and population characteristics (setting, gender, age, primary problem of sample)
- (iii) Sample size
- (iv) Measurement of trauma/PTSD
- (v) Measurement of psychosis
- (vi) Ethnicity (and proportions of ethnic groups in the sample)
- (vii) Relevant research finding i.e. studies that comment on comorbidity/prevalence rate of trauma/PTSD and psychosis by ethnic group
- (viii) Additional findings of interest e.g. comment on potential reasons for differences found if available

A qualitative synthesis according to the types of biases identified above will be commented on for all included studies.

Due to the variability in methodology (e.g. in measurement tools, primary population of focus) between the studies, and the criteria for 'exposure' and 'outcome' variables being

interchangeable, the synthesis and presentation of the findings were adapted to accommodate this.

4. Results

4.1 Search results

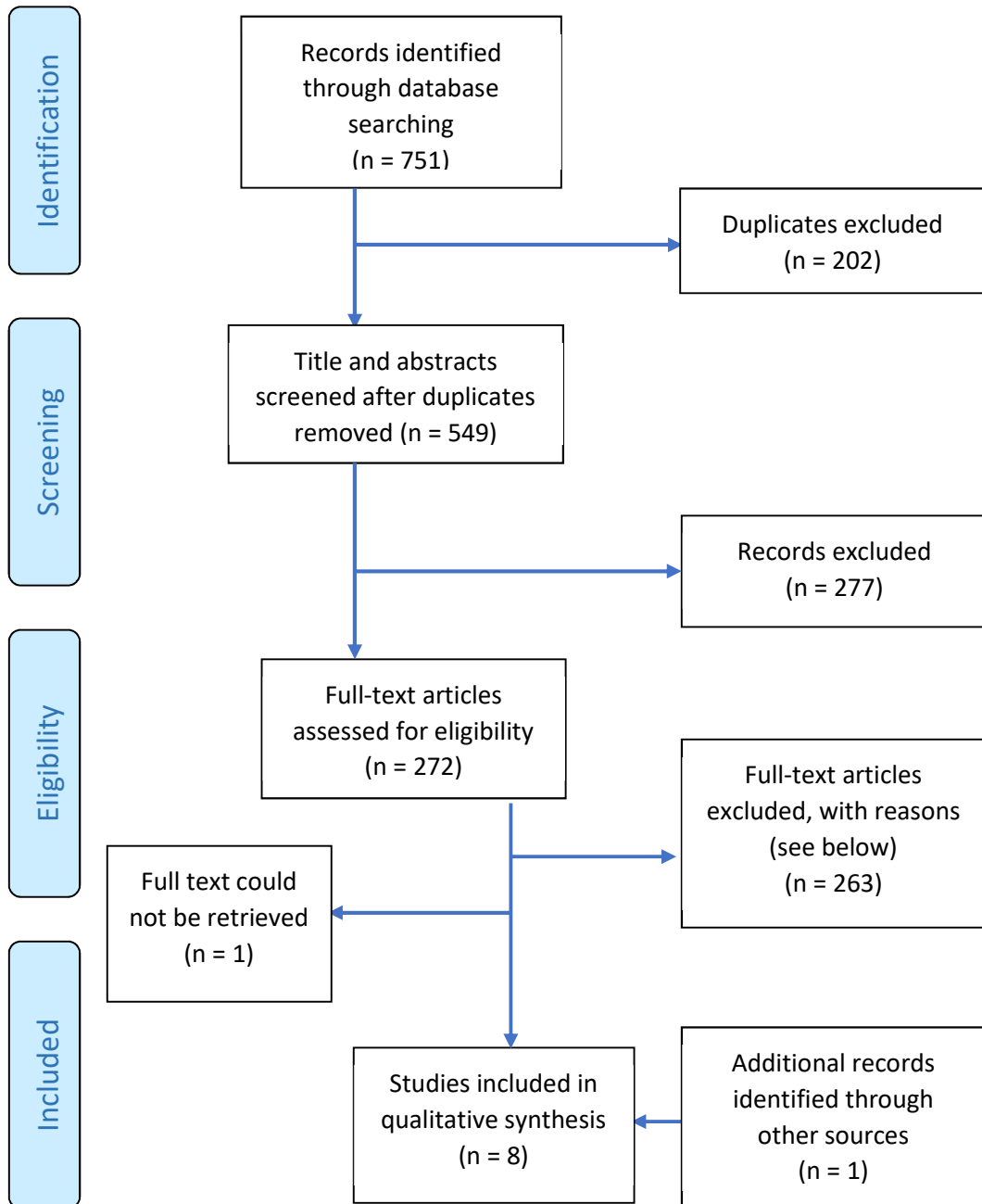


Figure 1: PRISMA flow diagram of study selection process

4.2 Overview of studies

Table 1. Extraction table summarising included studies in the review with quality scoring (studies in which psychosis was exposure variable)

Authors (year) and study site	Design/ period of data collection	Setting/ Population characteristics	Sample size (N)	Ethnic group studied (N, %)	Measure of trauma/PTSD & period of assessment	Measure of psychosis & period of assessment	Relevant findings	Additional findings of note	Quality score
Compton et al. (2004), Atlanta, USA	Cross-sectional Jan 2002 – Apr 2003	Sample divided by cannabis dependency and non-dependency inpatient psychiatric unit FEP, aged 18-30 Female (2, 11%); male (16; 89%)	18	African-American (18, 100%)	CTQ-SF - clinician administered Period: childhood	SCID-I (DSM-IV) to confirm diagnosis of schizophrenia & other psychoses Period: current	No control/other ethnic group, within same ethnic group: 16 with emotional abuse (89% prevalence) 11 with physical abuse (61% prevalence) 9 with sexual abuse (50% prevalence) 15 with emotional neglect (83% prevalence) 14 with physical neglect (78% prevalence)	Significantly higher scores of physical & sexual abuse in individuals with cannabis dependency than those without. Indication that patients with schizophrenia & cannabis dependency at significant greater risk of experiencing childhood trauma.	Fair

Authors (year) and study site	Design/ period of data collection	Setting/ Population characteristics	Sample size (N)	Ethnic group studied (N, %)	Measure of trauma/PTSD & period of assessment	Measure of psychosis & period of assessment	Relevant findings	Additional findings of note	Quality score
Posternak et al., (2005), Rhode Island, USA	Cross-sectional Period: 1995 - 2001	Adults presenting to psychiatric outpatient with diagnoses of MDD (private practice treating predominantly for medical insurance purposes) Mixed gender: proportions unspecified	1500 (749 diagnosed with MDD and used in analysis)	White (648, 87%); Black (31, 4%); Portuguese (23, 3%); Hispanic (22, 3%); Asian (5, <1%) other ethnic origin (20, 3%) (Latter two excluded i.e. exclude further 25 from analyses).	SCID-I (DSM-IV criteria) – rated by PhD psychologists or graduate research assistants Period: unclear	SCID-I (DSM-IV criteria) – diagnosis established if patient reported hallucinations or delusions with associated impairment or distress – rated by PhD psychologists or graduate research assistants Period: unclear	Rates of comorbid PTSD & psychosis in patients with MDD did not differ among ethnic groups with exception of Portuguese vs Hispanics who were less likely to be diagnosed with PTSD. Comorbid PTSD & psychosis (& MDD) rates were (Hispanic 7, 32%); White (14, 32%); Black (6, 19%); Portuguese (2, 9%).	Some evidence to suggest significant differences in rates of psychosis between Hispanic patients and White patients (27% vs 5%) even after controlling for confounding variables (27% vs 7%). Hispanic patients more likely to have comorbid psychosis & MDD than Portuguese patients (27% vs 4%), though cohorts differed on several demographic and clinical variables. No significant difference in rates of psychosis found between Black (16%) and Hispanic patients, nor in demographic and clinical profiles.	Poor
Sin et al., (2010), Singapore	Cross-sectional	Specialised service for Early Psychosis Intervention Programme (FEP sample) Female (31, 51%); male (30, 49%)	61	Chinese (51); others (10)	SCID-I (DSM-IV-TR). CAPS Period: unclear	SCID-I (DSM-IV-TR). PANSS Period: unclear	Ethnicity was associated with risk of PTSD with Chinese patients at lower risk. Rates of comorbid psychosis & PTSD were: Chinese group (7, 14%); vs other ethnic group (5, 50%).	The overall prevalence rate of PTSD in the sample was approximately 20%. No significant differences were found in demographic or clinical variable between individuals with or without PTSD.	Good

Note. FEP, First Episode Psychosis; CTQ-SF, The Childhood Trauma Questionnaire – Short Form; SCID-I, The Structured Clinical Interview for DSM-IV Axis I Disorders; MDD, Major Depressive Disorder; CAPS, The Clinician-Administered PTSD Scale; PANSS, The Positive and Negative Syndrome Scale.

Table 2. Extraction table summarising included studies in the review with quality scoring (studies in which trauma/PTSD was exposure variable)

Authors (year) and study site	Design/ period of data collection	Setting/ Population characteristics	Sample size (N)	Ethnic group studied (N, %)	Measure of trauma/PTSD & period of assessment	Measure of psychosis & period of assessment	Relevant findings	Additional findings of note	Quality score
David et al. (1999), Miami, USA	Cross-sectional Period of recruitment not stated	In-patient PTSD rehabilitation unit (elective admission) All male aged 26-63(Kinzie & Boehnlein, 1989) combat-veterans (48 Vietnam, 2 Korean, 2 Gulf & 1 Somalia war)	53	White (38, 72%), Hispanic (9, 17%), Black (6, 11%)	PTSD using SCID-I (DSM-III-R); M-PTSD & consecutive subgroup (n=24) completed DES + clinician interview to resolve queries Period: Current & lifetime	Psychosis using SCID (DSM-III-R) + clinician interview to resolve queries Period: Current & lifetime	Psychotic symptoms more common in minority groups - 83% (5) blacks, 67% (6) Hispanics, 26% (10) whites.	Association of psychotic symptoms in combat related PTSD & comorbid major depression more common in ethnic minority veterans group (11 of 21, 52% vs 4 of 32, 13%). Psychotic symptoms were associated with the presence of current MDD. All patients with psychotic symptoms had hallucination reflecting combat-related themes.	Poor

Authors (year) and study site	Design/ period of data collection	Setting/ Population characteristics	Sample size (N)	Ethnic group studied (N, %)	Measure of trauma/PTSD & period of assessment	Measure of psychosis & period of assessment	Relevant findings	Additional findings of note	Quality score
Hamner et al., (1999), USA	Cross-sectional Period of recruitment not stated	All male Vietnam veterans, outpatients or inpatients meeting DSM-IV criteria for PTSD Aged 41-60	45	African American (22, 49%); Caucasian (23, 51%)	CAPS - clinician administered (DSM-III-R) Period: current	PANSS to assess symptom severity. SCID-P – psychotic screen module (for evidence of hallucinations, delusions) – (DSM-III-R) or thought disorder by MSE. Excluded psychotic symptoms occurring during flashbacks or dissociative period. Period: current (excluded historical)	22 PTSD patients had psychotic features (PTSD-P). 68% (15) African American PTSD patient had positive psychotic symptoms (7 AA had no psychotic features) vs 30% (7) White PTSD patients with comorbid psychotic features (16 W had no psychosis). There were significantly more African-American patients than Caucasian in the PTSD-P group as opposed to the nonpsychotic group (64% vs. 32%, $\chi^2 5.9.56$, $p = .01$)	All 22 PTSD-P had hallucinations in at least one modality. For 17 of these individuals, the content of hallucinations involved both combat- and non-combat-related themes. 19 patients had delusions, only 1 patient with combat-related theme. Only 1 patient had formal thought disorder. All PTSD-P obtained at least a 4 (moderate severity) on one of the four PANSS critical items. CAPS scores were significantly higher in PTSD-P patients with MDD than those without. PANSS total and negative score higher in PTSD-P patients with comorbid MDD.	Fair

Authors (year) and study site	Design/ period of data collection	Setting/ Population characteristics	Sample size (N)	Ethnic group studied (N, %)	Measure of trauma/PTSD & period of assessment	Measure of psychosis & period of assessment	Relevant findings	Additional findings of note	Quality score
Heffernan et al. (2015), Queensland, Australia	Cross-sectional Period: May – June 2008	In custody (high security correctional centres), Female (65, 16%; mean age – 29); male (331, 84%; mean age – 31)	419 (396 used for analysis)	Indigenous Australians: Aboriginal (317, 80%); Torres Strait Islander people (32, 8%); Individual identified as both (46, 12%)	CIDI 2.1 module (& standard CIDI module for other extreme stressful or upsetting events) – (ICD-10) Period: 12 month prevalence	CIDI used to screen positive response then followed up with psychiatric interview. Diagnosis confirmed by panel (ICD-10) Period: unclear	No control/other ethnic group, within same ethnic group: For 25% of the sample, PTSD was associated with co-occurring psychosis.	12 month prevalence of PTSD was approximately 15% (12% in males and 32% in females – significant difference). Individuals with PTSD were significantly more likely than those without PTSD to experience any mental disorder (31% with anxiety, 33% with depression), 75% with substance use disorder. PTSD associated with poorer outcomes e.g. access to health care and risks of recidivism.	Poor

Authors (year) and study site	Design/ period of data collection	Setting/ Population characteristics	Sample size (N)	Ethnic group studied (N, %)	Measure of trauma/PTSD & period of assessment	Measure of psychosis & period of assessment	Relevant findings	Additional findings of note	Quality score
Kinzie et al., (1989), USA	Case series Period: Between 1982 - 1987	Cambodian refugees aged 18 – 65 who were consecutive inpatients in psychiatric clinic for Indochinese refugees Female (66, 66%); male (34, 34%) of whom	100 (7 cases detailed in paper; of whom 5 female and 2 male)	Cambodia (100, 100%)	DSM-III-R definition of PTSD Method of assessment: unclear but possibly through interviews during course of treatment Period: unclear	DSM-III-R definition of psychosis Method of assessment: unclear but possibly through interviews in course of treatment Period: unclear	No control/other ethnic group, within same ethnic group: 7% presented with psychosis (DSM-III-R), meeting criteria for either schizophrenia (n = 6) or schizoaffective (n = 1).	Psychotic symptoms for the 7 patients were neither brief nor transient and was in addition disruptive to functioning. An individual not included in the 7 patients detailed in report was diagnosed with schizophreniform disorder and did not show evidence of psychosis at contact 3 year later. 100% of those with psychosis hospitalised compared to 7.5% of those without psychosis. Patients with and without psychosis did not differ in demographics or by quantity of trauma experienced.	Poor
Monnier et al., (2002), USA Period: September 1995 – June 1997	Cross-sectional	All male veterans aged >17 diagnosed with PTSD in outpatient program for combat-related assessment & treatment (gender unspecified)	124 (111 used in analysis)	Caucasians (71, 64%); African American (40, 36%)	All diagnoses reached by consensus (using chart review, interviews, self-report, CAPS-1 and M-PTSD) Period: unclear but trauma history not assessed	Non-standardised clinical interviews Period: unclear	African American (9, 23%) veterans were more likely to be diagnosed with co-morbid psychotic disorder than Caucasians (3, 4%) despite similarities in PTSD symptom manifestation and general psychopathology.	There were no racial differences of PTSD symptoms and general psychopathology (e.g. anxiety and depression). 12% of whole sample diagnosed with psychotic disorder.	Poor

Authors (year) and study site	Design/ period of data collection	Setting/ Population characteristics	Sample size (N)	Ethnic group studied (N, %)	Measure of trauma/PTSD & period of assessment	Measure of psychosis & period of assessment	Relevant findings	Additional findings of note	Quality score
Odenwald et al., (2009), Somalia	Cross-sectional Period: August – December 2003	Active combatants in Somalia (convenience sampling) Female (882, 11%); male (7242 89%)	8723 (8124 inc in analysis)	Somali (8124, 100%)	Somali version of modified PDS – self-report Period: unclear	Paranoid ideation using CIDI item G4 Period: unclear	No control/other ethnic group, within same ethnic group: The rate of paranoid ideation was 26% in respondents with PTSD and 4% among those without PTSD.	Overall prevalence of paranoid ideation was 5% (396 veterans). Paranoid ideation found in 396 respondents. Functional drug use to control PTSD was significantly associated with increased likelihood of paranoia. Men were more likely than women to present with PTSD, paranoia and more often use khat.	Poor

Note. SCID-I, The Structured Clinical Interview for DSM-III-R Axis I Disorders; M-PTSD, Mississippi Scale for Combat-related PTSD; DES, Dissociative Experiences Scale; MDD, Major Depressive Disorder; CAPS; The Clinician-Administered PTSD Scale; PANSS, The Positive and Negative Syndrome Scale; SCID-P, The Structured Clinical Interview for DSM-III-R with Psychotic Screen; CIDI 2.1, Composite International Diagnostic Instrument version 2.1; PDS, Posttraumatic Stress Diagnostic Scale.

Table 1. and Table 2. summarises the details of all included studies in the current review. Nine studies were identified as meeting the eligibility requirement for the review question (see PRISMA flowchart, Figure 1.): eight cross-sectional and one case study series. Of these, one cross-sectional study (Hamner et al., 1999) was identified by screening the reference list of included studies in a previous case illustration and literature review (Adekola, Leso, Dewan, & Johnson, 2003). Studies were mainly conducted in the USA ($n = 6$), and at least one study in Australia, Somalia and Singapore. Papers were published between 1989 and 2015. The sample sizes of eligible studies ranged from seven to 8124, and included varying sample populations (e.g. inpatients, refugees, outpatients, specialised treatment centres), and primary clinical presentations (e.g. PTSD, psychosis, or other psychiatric diagnoses). There were also a number of other methodology variations used to define and operationalise all the relevant concepts required for this review (e.g. reflected in the notable differences in type of measures, use of structured interviews vs self-reports, categorisation of ethnicity, diagnostic classifications referenced and so forth). In relation to ethnic groups studies, six papers compared between different ethnic groups whilst, three identified only a single ethnic group. The heterogeneity of these studies therefore poses a challenge in the comparability of the findings and conclusions, and the implication of this are considered in detail within the discussion. In addition, given that the number of papers identified were small and definitions of all the required concepts and methodology varied, a meta-analysis would not be valid or reliable.

4.3 Relevant study findings – are there ethnic variations for the coexistence of trauma/PTSD and psychosis?

The main focus of the synthesis was to investigate whether there were ethnic variations in the experience of comorbid trauma/PTSD and psychosis. For clarity, the included studies were examined on the basis of which disorder was the exposure or outcome variable in the paper i.e. whether trauma/PTSD; or psychosis or other focus was primary topic. Of the nine studies

identified for this review, two looked at a group with psychosis and reported on experience of trauma or comorbid PTSD (see Table 1.), and six looked at traumatised or PTSD sample and examined the rate of psychosis or psychotic symptoms (see Table 2.). One paper (Posternak & Zimmerman, 2005) did not have either disorder as its primary focus (the paper investigated Major Depressive Disorder; MDD), however, they examined the rate of PTSD in individuals who had been diagnosed with comorbid psychosis (and MDD). Therefore, this paper was analysed as a psychosis exposure paper.

4.3.1 Prevalence rate of trauma/PTSD in psychosis

Only one study looked at the prevalence of trauma in relation to psychosis (Compton et al., 2004). They found in a sample of African Americans with a FEP that emotional abuse (89%) was the most reported form of childhood trauma, followed by emotional neglect (83%); physical neglects (78%); physical abuse (61%); with sexual abuse (50%) as least prevalent. However, this study did not examine a control or other ethnic group in their paper.

The remaining two papers, (Posternak & Zimmerman, 2005) and (Sin et al., 2010) reported the rates of PTSD in psychosis. Both studies demonstrated ethnic variations in the rates of comorbid PTSD in individuals with psychosis. Posternak and colleagues (2005) found differences in rate of co-occurring PTSD and psychosis (and MDD) was significantly higher in the Hispanic group (32%) when compared to Portuguese sample (9%). Sin and colleagues (2010) found that the Chinese sample (majority ethnic group; 14%) in their study were less likely to be diagnosed with comorbid PTSD than other ethnic groups (50%) in a population of FEP individuals.

4.3.2 Prevalence rate of psychosis in PTSD

Of the six studies looking at the prevalence of psychosis in traumatised or PTSD samples, three papers compared the rates between different ethnicities (David et al., 1999; Hamner et al., 1999; Monnier et al., 2002), whilst the others looked at a uniformed ethnic group (Heffernan et al.,

2015; Kinzie & Boehnlein, 1989; Odenwald et al., 2009). The majority of these studies were conducted with veterans or individuals in combat ($N = 4$). Only one study investigated the experience of refugees (Kinzie & Boehnlein, 1989).

All the studies comparing different ethnic groups demonstrated ethnic variations in the rates of comorbid psychosis with PTSD, finding that the ethnic minority groups were more likely to endorse such experiences. They identified prevalence of comorbid psychosis and PTSD ranging from 4% - 83%. The rates of psychosis in the three studies investigating a common ethnic group ranged from 7% - 26% with variation in the setting, sample population, country and ethnic groups studied.

4.4 Additional findings

4.4.1 Possible explanations for trauma/PTSD outcome in psychosis samples

There were some interesting findings in the studies which looked at rates of trauma/PTSD in their psychosis sample. One paper indicated that affective processes may compound the relationship between trauma/PTSD and psychosis (Posternak & Zimmerman, 2005). That is, experience of trauma/PTSD or psychotic symptoms were more common in psychotic individuals who reported comorbid emotion regulation difficulties or depression. Whilst Compton and colleagues (Compton et al., 2004) proposed that cannabis dependency was associated with a higher risk for experiencing childhood trauma. They also found possible gender differences, as they highlighted that the only two females in their sample were both in the cannabis dependency groups. When analyses were conducted after removing the female participants, the differences in sexual abuse was no longer significant between the non-dependent and dependent cannabis groups. Sin and colleagues (Sin et al., 2010) on the other hand did not find any significant differences in demographic or clinical variable between individuals diagnosed with and without PTSD.

4.4.2 Possible explanations for psychosis outcome in PTSD samples

Three papers in this section proposed mood difficulties as a possible confounder in the relationship between trauma/PTSD and psychosis, suggestive of interaction effects. Comorbid depression was associated with greater severity of psychotic symptoms and overall more complex presentations (David et al., 1999; Hamner et al., 1999; Heffernan et al., 2015). However, no differences were found between ethnic groups in terms of depression, anxiety or PTSD symptomology in another study (Monnier et al., 2002). Instead, Monnier and colleagues highlighted potential predisposition in clinicians to diagnose psychosis in their African American individuals than Caucasians accounted for the differences in elevated rates in the African American group despite contrary evidence. Odenwald and colleagues (Odenwald et al., 2009) cited that comorbid functional drug use (khat) was associated with paranoid ideation in their PTSD sample. In addition, gender difference were revealed in relation to paranoid ideation, PTSD symptomology and functional khat use, with men being more likely to endorse all these aspects than women. Kinzie and colleagues (Kinzie & Boehnlein, 1989) were unable to explain the reason for the development of psychosis in some individuals but not others given that the experience of trauma was quantitatively similar in their sample. They proposed several reasons for this, for example they suggested that ongoing adversity, experience of stigma and worse coping resources may help to explain why some individuals who have been severely traumatised go on to develop psychosis.

4.5 Quality assessment of reviewed studies

Of the identified studies, six studies received a poor quality rating, with two studies deemed as fair and one study received a good rating. There were additional items relating to measurement of trauma/PTSD, psychosis and conceptualisation of ethnicity, although these scores were not included in the overall quality rating of the studies.

4.5.1 Poor quality studies

All the poorly rated papers, with the exception of one (Posternak & Zimmerman, 2005), were from studies which looked at a traumatised or PTSD sample and investigated the rate of psychosis. All the papers in this group did not have a follow up period nor did they measure the exposure of interest prior to the outcome variable as they were all cross-sectional studies, with exception of one (Kinzie & Boehnlein, 1989), which was a case series with follow up, however the details of this were not clear in their report. In addition, this paper was the only study which failed to state the clearly their research objective. All the authors of each paper were not blind to the exposure status of their participants, did not examine different levels of the exposure as related to the outcome and in addition only measured the exposure variable over one time point. All papers clearly specified the period of recruitment, except for one (David et al., 1999), although the paper did state that all participants were recruited as part of consecutive admissions. In terms of reporting participation rates, only one paper (Heffernan et al., 2015) specified or reported whether participation of eligible individuals approached to take part in their study reached at least 50%. Three studies (Monnier et al., 2002; Odenwald et al., 2009; Posternak & Zimmerman, 2005) did not uniformly apply their exclusion criteria to all participants as they also excluded some individuals from analysis, mostly due to small sub-sample size in a particular ethnic group. None of the papers reports justification of the size of their sample or included power calculations for their analysis. The loss to follow-up criteria were largely not applicable to the studies as they were cross-sectional studies. In relation to this criteria, it was difficult to determine this in the study by Kinzie and colleagues (Kinzie & Boehnlein, 1989). Heffernan and colleagues (Heffernan et al., 2015) was the only study to adjust for potential confounding variables in their analysis.

In relation to the addition criteria items relating to the measurement of the trauma/PTSD and psychosis and the categorisation of ethnicity, there were some variability

between the studies. Two studies (David et al., 1999; Heffernan et al., 2015) received a good rating for their measurement of both PTSD and psychosis as they conducted interview using standardised measures with a clinician, and additionally David and colleagues clarified queries by consensus. However, both failed to score maximum points on their categorisation of ethnicity. The study by David and colleagues score zero points as it used very simplified categorisation of ethnicity (e.g. White, Black, and Hispanic) and the paper by Heffernan and colleagues failed to reach maximum point scoring a one as it condensed all the Aboriginal ethnic groups into one although the participants identified themselves in three sub-groups. Monnier and colleagues (2002) received a good rating for their measurement of PTSD having used interviews by clinicians and consensus to diagnose participants. All remaining studies failed to reach the maximum score for their measure of psychosis having relied mostly on self-report or non-standardised measures or conducting diagnoses with non-experts trained workers or students. They also failed to reach maximum scoring on their categorisation of ethnicity having used simplified groupings or condensing distinct sub-groups into one.

4.5.2 Fair quality studies

Two studies (Compton et al., 2004; Hamner et al., 1999) received a fair rating in terms of their quality. The study by Compton and colleagues fared better than the paper by Hamner and colleagues, receiving a good rating for clearly defining the study population, reporting the participation rate of eligible participants and using a sufficient timeframe to examine at associations between exposure and outcome. Hamner and colleagues paper received a good rating in relation to implementing the independent and dependent variables consistently across all study participants, using valid and reliable standardised measures, whereas the paper by Compton and colleagues did not. Both studies failed on quality in relation to appropriate sample size justification and power analysis; not examining the exposure of interest prior to measurement of the outcome variable; assessing the outcome over one time point; non-blinding

for analysis; and adjusting for key potential confounders in their analyses. Loss of follow-up criteria was not applicable to both studies as they were cross-sectional, and this also meant that neither study assessed the exposure variable more than once over time. A good rating was received by both papers on all other quality criteria.

When considering the additional items to assess quality of measurement, Hamner and colleagues paper (1999) achieved a good rating for its measurement of both PTSD and psychosis and a fair rating for ethnicity categorisation due to its simplified use of ethnic groups (e.g. 'Caucasians'). Compton and colleagues (2004) assessment of psychosis was good, but poor for PTSD and fair for ethnicity.

4.5.3 Good quality studies

Only one paper (Sin et al., 2010) received a good quality rating. The paper failed on quality in relation to specifying their participation rate of eligible individuals was at least 50%; sample size justification and power analyses; measurement of exposure prior to outcome; sufficient time frame for examining associations; assessing exposure only once over time; and non-blinding for purpose of analyses. Similarly, to the other cross-sectional the loss to follow-up criteria was not applicable.

In relation to the additional criteria, this study scored one in relation to its measurement of psychosis and PTSD, having relied on a 'single trained interviewer' to diagnose both disorders. The study oversimplified their categorisation of ethnicity, grouping one group as 'others'.

5. Discussion

The aim of the current study was to review all published, original studies reporting the prevalence of con-occurring trauma/PTSD and psychosis within defined ethnic group populations. There was also an additional aim to highlight evidence (if available) on the possible hypotheses and mechanisms if such variations by ethnicity exists.

5.1 Summary of findings

Due to the varying methodologies of the included studies, it was not possible to draw firm conclusions regarding the objectives of the review question. However, a consistent pattern was identified in the papers looking at the rates of psychosis in PTSD. Of the papers which studied different ethnic groups (David et al., 1999; Hamner et al., 1999; Monnier et al., 2002), they all demonstrated that the ethnic minority groups with PTSD were more likely to experience psychotic symptoms, albeit using different categorisations of ethnicity (e.g. White vs Caucasian; Black vs African America). Interestingly all these studies were conducted in the USA and with combat-veterans. The remaining papers (Heffernan et al., 2015; Kinzie & Boehnlein, 1989; Odenwald et al., 2009) looking at this relationship conducted their research with a common ethnic group and it is difficult to interpret whether the rates of psychotic symptoms identified in individuals presenting with PTSD was more elevated, similar or reduced without comparison to a control or other ethnic group. Although, Heffernan and colleagues highlighted the relatively high rates of PTSD as well as comorbid disorders in their sample of Indigenous Australians than in the general Australian population (where the study was conducted). The prevalence rates reported for comorbid PTSD with psychotic symptoms ranged from 7% - 83%, varying by ethnic group, country and population studied.

In relation to the studies which investigated the rates of PTSD in psychosis, one study found a similar pattern in that the ethnic majority group was less likely to endorse co-occurring PTSD symptoms (Sin et al., 2010). Another study (Posternak & Zimmerman, 2005) found contradictory evidence, showing that there were no ethnic variations in the rates of comorbid PTSD and psychosis, with the exception of two ethnic groups. When comparing the Portuguese and Hispanic groups, they found that the latter group were more likely to be diagnosed with

comorbid PTSD. Additionally, psychosis was also more elevated in the Hispanic groups. It is difficult to interpret these findings as both ethnic groups could be considered to have minority status in the study site and the paper further found demographic and clinical differences between the groups which may explain the varying rates. The remaining paper (Compton et al., 2004) did not have a control group or comparison ethnic group but found high rates (50% - 89%) of different types of childhood abuse in their African American sample experiencing FEP. Additionally, severity of abuse, particularly physical and sexual was associated with cannabis dependency, indicating that this elevated the risk of severe childhood trauma in those individuals.

None of the identified papers explicitly cited putative hypotheses or mechanisms for variations by ethnic groups when these were highlighted. Instead potential mechanisms were proposed to explain the associations between trauma/PTSD and psychosis more generally. Comorbid depression was implicated and interacted with the association between trauma/PTSD and psychosis in four studies (David et al., 1999; Hamner et al., 1999; Heffernan et al., 2015; Posternak & Zimmerman, 2005). Other studies highlighted the potential of comorbid drug use complicating the interaction between trauma/PTSD and psychosis (Compton et al., 2004; Odenwald et al., 2009). Frequent drug use or dependency was associated with greater risk of trauma/PTSD and/or psychotic symptoms. Although gender was not a focus of this review, some of the papers highlighted differences between groups according to this demographic (Compton et al., 2004). Whilst some papers extrapolated reasons for the variations between trauma/PTSD and psychosis, others were more speculative suggesting a number of factors related to wider social and clinical context (Kinzie & Boehnlein, 1989; Monnier et al., 2002). Moreover, one study did not find any demographic nor clinically significant differences to explain associations.

Overall, there is very little research exploring comorbidity of trauma/PTSD and psychosis and variations by ethnic group. Much of the research findings are tentative and are likely to be artefacts of the methodological approaches. Heterogeneity between the studies also make it more difficult to interpret the results and compare findings. Thus, the relevance of the findings will be critiqued whilst considering the quality of the methodology.

5.2 Methodological issues and quality factors of included studies

The current review has some limitations. This is a difficult area of research given the issues highlighted above. In particular, PTSD and psychosis considerably overlap in terms of symptoms which can often contribute to difficulties for clinicians and researchers to distinguish between them. These issues demonstrate the complex nature of systematically reviewing this topic area and perhaps the reason it is so under-researched.

Other significant methodological issues have been highlighted within the review of the literature in this topic area. Firstly, very few papers examined the prevalence of comorbid trauma/PTSD and psychosis by ethnicity. Of the papers that looked at this, findings remain largely inconclusive given the variations in methodology applied to the study. In addition, the majority of the papers received a poor quality rating in light of methodological flaws which further puts in question the results that can be gleaned from those studies. As the majority of studies were cross sectional in nature and failed to achieve adequate ratings (e.g. in relation to power to detect differences, blinding of subjects and measurement over different time points), all factors which can lead to several biases, and thus makes their findings difficult to interpret. For example, failure to specify details of recruitment and refusal rates may introduce selection biases which may artificially inflate or deflate ethnic difference where none are present. Furthermore, selection bias may make it difficult to determine whether the participants of the study are representative of the local population.

Studies were not epidemiological in nature nor were they primarily focussed on prevalence of comorbidity and thus may have over- or underestimated the rates reported. The majority of the studies were cross-sectional, therefore, only taking account of a specific snapshot in measuring the prevalence of comorbidity. This makes it difficult to consider whether these estimates change over time, and put into question whether they are reliable and valid. This issue is also problematic as psychotic symptoms may well lead or cause a PTSD response and given the phenomenological similarities between the two disorders, may make distinguishing symptomology difficult and challenging. The absence of power calculations, small sample sizes in the majority of papers and studies without comparison groups further make the findings of this review hard to interpret. For example, it would be difficult to state whether the rates found were higher or lower than expected and if certain ethnic groups are more at risk of comorbidity than others. One possible solution would be to conduct very long follow-up studies, however these tend to be avoided due to the costs and ethical dilemmas which present from conducting prospective longitudinal research of relatively low incidence disorders (Fisher et al., 2011).

Furthermore, the experience of trauma, PTSD and psychosis can be difficult to capture, particularly given the phenomenological similarities between the disorders as highlighted by examples above. In addition, prevalence of other disorders such as depression are high in both populations (traumatised/PTSD and psychosis) and may mask symptoms, particularly negative symptoms of psychosis (Kessler, Chiu, Demler, & Walters, 2005; Kirkpatrick, Buchanan, Breier, & Carpenter Jr, 1994). Indeed, nearly half of the included studies found that the presence of depression complicated the interpretations which could be drawn about the association between trauma/PTSD and psychosis. However, given the poor quality rating of the majority of the studies, these findings should be gleaned with caution. Furthermore, the measurement of both disorders at the same time period, as conducted in all the eligible studies, complicate

matters further in deciding which experience or disorder is primary or secondary. These issues can create problems in accurate diagnosis and detection of individuals presenting with these experiences. The chronology of disorders in comorbid diagnosis is an important to consider when investigating prevalence rates. Some trauma may well include psychosis-related events and psychotic individuals may develop PTSD as a consequence of psychosis symptoms (Berry, Ford, Jellicoe-Jones, & Haddock, 2013). None of the eligible studies, with the exception of one paper (Kinzie & Boehnlein, 1989) differentiated between such experiences. Biases are further introduced in the analysis as researchers were not blind to the exposure of participants. Whilst on the whole, most of the studies utilised standardised and validated measures to assess individuals, most of these were not conducted by clinicians in the field, which arguably represent poor quality assessments and some relied wholly on self-reports. The gold standard of such assessment should ideally include standardised, validated diagnostic semi-structured interviews, administered by clinicians or expert researchers and if possible supplemented with consensus discussions. Some papers in the review were deemed of high quality with respect to their assessment of PTSD (David et al., 1999; Hamner et al., 1999; Heffernan et al., 2015; Monnier et al., 2002) and psychosis (David et al., 1999; Hamner et al., 1999; Heffernan et al., 2015). In addition, the conceptualisation of these notions differed in terms of diagnostic iterations utilised, period of measurement and in the methods used to assess these experiences between the studies. Such variations introduce heterogeneity and potential for bias, therefore making comparisons problematic. The reliance on retrospective self-report of traumatic experiences may create further difficulty, partly due to cross-cultural explanations of mental health disorders and trauma but also possible distortions in memory and/or difficulties individuals may experience in disclosing their experiences (Berg et al., 2015; Roy & Perry, 2004). With respect to this, it is important to note that although retrospective methods have been criticised for being unreliable, particularly with psychotic individuals and nature of these symptoms, some authors investigating this issue have found no evidence that these methods

increase biases in memory or that they are compounded by mental illness (Fisher et al., 2011). Moreover, research generally supports the validity and reliability of assessing trauma experiences and PTSD within psychosis populations (Goodman et al., 1999; Mueser et al., 2004; Resnick, Bond, & Mueser, 2003). Instead, the indication is that unreliable reports are a product of under-reporting or cross-cultural differences in subjective perceptions or definitions of experiences considered as trauma (McFarlane, Schrader, Bookless, & Browne, 2006; Picken, Berry, Tarrier, & Barrowclough, 2010; Thombs et al., 2007). Nonetheless, the detection and assessment of these somewhat complex, overlapping experiences and disorders is a key limitation within the literature and may account for inconsistent or unreliable findings.

The definition of ethnicity within the literature is an additional methodological issue. Firstly, ethnicity was operationalised in differing ways, for some studies it was synonymous with race, others grouped individuals based on sharing common region of origin or culture and some identified distinct ethnic groups. Whilst none of these methods are problematic and can all be used as valid representations of ethnicity, it creates difficulties in meaningful comparisons in a review of this kind. Nonetheless, ethnicity, race and culture are related but distinct concepts (McKenzie et al., 2008). In addition, some studies condensed ethnically diverse groups when analysing the evidence which poses potential of introducing biases. Experiences may differ between these groups, thus grouping of this kind may overinflate or underestimate findings of comorbidity. The paper by Morgan and colleagues (2006) highlights the problem this can create. They found that the African-Caribbean individuals in their sample were at even greater odds of increased risk of psychosis than the African participants when both groups were independently compared to their White British counterparts. This finding demonstrates how condensing these distinct groups as Black may confound results. Thus crude categorisations of this kind are not ideal may lead to indistinguishable conclusions (McKenzie et al., 2008).

5.3 Consideration of the literature

Studies investigating co-existing experiences of trauma/PTSD and psychosis, demonstrated some support for differential presentations by ethnicity, although the topic area is relatively under-researched (David et al., 1999). For example, psychotic symptoms in PTSD were noted to be more common in Hispanic veterans (David et al., 1999). Wilcox and colleagues (1991) corroborated these findings and found that Hispanic ethnicity, but not other factors such as length of combat exposure, was associated with lifetime prevalence of auditory hallucinations in veterans with PTSD. In a sample of psychosis patients, Berg and colleagues (2015) found that ethnic minorities reported significantly more childhood trauma than patients from ethnic majority sample, corroborating the findings by Compton and colleagues (Compton et al., 2004). This finding is contrary to evidence presented by Aakre and colleagues (2014). They found that in a group of women with substance use disorders (SUD), the Caucasian participants with comorbid schizophrenia were more likely to meet criteria for PTSD than the African American sample. These contrary results are pointers to the pertinent need for reviewing the influence of ethnicity in these disorders in future research.

Only one study in this review looked at the association between trauma/PTSD and psychosis in a refugee sample (Kinzie & Boehnlein, 1989). Refugees form a unique group of individuals in that their experiences may be impacted on by migration as well as exposure to trauma which is usually documented in their history and the main reason for migrating (Parrett & Mason, 2010). They are also likely to be ascribed an ethnic minority status in their host country and may be more likely to experience adverse events post-migration (Connelly & Schweiger, 2000). Thus, their experiences in relation to this topic is also pertinent. Refugees have been reported to be at high risk of negative psychological outcomes such as suicide, depression, substance misuse as well as psychosis and PTSD (Fazel, Wheeler, & Danesh, 2005; Lavik, Hauff, Skrondal, & Solberg, 1996; Ramsay, Gorst-Unsworth, & Turner, 1993; Turner, Bowie, Dunn,

Shapo, & Yule, 2003). It may be that post-migration difficulties compound pre-experiences of trauma and thus increase the risk of developing psychiatric disorders (Burnett & Peel, 2001). However, it is important to note that refugees form a heterogeneous group varying in relation to cultural backgrounds and their pre- and post-migration experiences, thus caution must be taken not to generalise (Lavik et al., 1996). There are also concerns related to the application of Western diagnostic assessment across cultures, particularly among refugees which may compound difficulties with validity of diagnoses (Watters, 2001).

6. Conclusions

Our finding of a possible effect of ethnicity on the rates of comorbid PTSD and psychosis is interesting. This paves the way in thinking about the potential reasons of why such variations exist. This observation may be due to a greater likelihood of comorbidity in ethnic minority groups due to increased risk of exposure to trauma and adverse environments. It is also important to understand these relationships as they could have significant clinical implications. It is plausible that trauma or PTSD may complicate the clinical presentation of psychosis and be associated with greater, more complex needs and vice versa. Furthermore, the experience of developing psychosis and its treatment methods may further elevate risk of exposure to psychosis-related trauma or development of PTSD (Shaw, McFarlane, Bookless, & Air, 2002; Sin et al., 2010). However, it is sensible not to overstate the potential relevance of these findings as clearly more research on the ethnic profile in comorbid trauma/PTSD and psychosis is required. The differences between the studies in definition and methodology make comparison difficult and with a majority of poor quality papers, the results should be interpreted with caution.

The conclusions that can be drawn for this review are still in its infancy given that very few studies have systematically looked at this topic area or even considered it in their research.

Thus, only tentative conclusions can be drawn. The synthesis suggests that high quality studies that formally assess both trauma, PTSD and psychosis whilst looking at the influence of key demographic information such as ethnicity are required. Therefore, the recommendations of this review would be to improve methodological quality of future studies in order to improve the robustness of the findings and encourage consistency in research aims and methods. It is a priority to employ higher quality studies to identify whether comorbid trauma or PTSD and psychosis vary by ethnicity, and to establish the potential factors accounting for this variation as they may provide a promising new direction for developing innovative psychosocial interventions for people affected by these difficulties.

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8. Appendix

8.1 Parameters for concept 1: Psychosis/psychotic symptomology

The concept of psychosis for the purpose of this review included first episode psychosis, as well as acute or chronic presentations, and individuals with concurrent diagnosis of another psychiatric disorder. Studies were considered if valid measures were used to assess potential psychotic disorder and/or psychotic symptomology (e.g. paranoia, hallucinations, delusions, and thought disorder) and these symptoms met or were above clinical cut-offs when no formal diagnoses were given to the samples studied. For this reason, search terms relating to mainly the positive symptoms of psychosis were included. Studies investigating 'at-risk' or 'ultra-high risk of psychosis' groups who have not developed psychosis or individuals experiencing 'psychotic-like' symptoms or so called 'psychotic experiences' were excluded. Additionally, where psychosis or psychotic symptomology overlapped with or were secondary to other psychiatric presentations (e.g. mood disorders), these studies were included if they reported the comorbidity of psychotic symptoms and trauma/PTSD by ethnic groups. The purpose of inclusion of such studies were considered due to the overlap of many psychiatric disorders with psychosis which are not necessarily explicitly examined even in studies where psychotic disorders may be the primary focus. Studies examining schizotypy, personality traits or disorders (e. g. schizotypal or paranoid personality disorders (PD)) were excluded. Exclusions are justified on the basis that these constructs do not fall under psychosis term or schizophrenia spectrum conditions.

8.2 Parameters for concept 2: Trauma/PTSD

In light of considerable overlap in terminology and measurement in relation to environment stressors, adverse or stressful 'life events' was included in search terms to ensure all literature relating to traumatic experiences were captured. Life events have been viewed and defined in a number of different ways, for example as, life stresses; severe and major events; victimisation and traumatic experiences. However, it is important to note that traumatic events are simply not stressful life events (McManus et al., 2009). Life events for the purpose of this review were not considered trauma unless they referred to traumatic experiences. Thus, studies which looked at adverse life events (e.g. divorce) without differentiation (in reports or statistical analysis) of other events (e.g. death of a family member) which could be considered as a trauma or could be encapsulated by both terms were not included. Although studies which diagnosed PTSD (including individuals with concurrent diagnosis of another psychiatric disorder) in their sample were included to broaden the breadth of research examined as trauma is a prerequisite to PTSD diagnosis. PTSD was considered as specified diagnosis made by clinicians and/or researchers in line with diagnostic manuals used at the time of the study or clinical judgement. Studies were included if they used valid measures to diagnosis PTSD in their sample. Where symptomology of PTSD (e.g. dissociation) were reported without specific diagnosis of PTSD, these studies were not included given possible overlap with other psychiatric disorders (e.g. psychotic symptoms). Though it is worthy of note that there still may be overlap between PTSD and psychotic symptomology. For instance, individuals diagnosed with PTSD may report hallucinatory experiences which may or may not relate to their experience of trauma. This

potential overlap was considered on a case-by-case basis for included studies. Similarly, as highlighted above for the psychotic disorders, PTSD was considered whether it was the primary or secondary clinical presentation, as this too has potential of overlap with many psychiatric disorders.

Although the concept of PTSD as a diagnosable psychiatric disorder was only recognised formally for the first time within the DSM-III (American Psychiatric Association, 1980), no date restrictions was applied to the searches. In addition, the trauma string was included to ensure identification of the all literature relating to traumatic experiences (in whichever way these were described in the articles)

8.3 Information sources and search strategy

Keyword searches as well as subject headings applied (with inclusion of different subject headings due to differences in MESH terms between the databases used) were used. For instance, for the concept of ethnicity, the subject heading for MEDLINE and PsycINFO were slightly different. Subject headings were expanded to increase the breadth of the literature identified as this ensures all related and relevant terms under each heading are included. As WoS does not use subject heading terms, all the terms for this database were run as keyword searches i.e. searching for the terms in any part of the article. The wildcard symbols (with the use of asterix * or question mark '?' to replace unknown characters) was used to allow variations in spelling and where there was more than one word in the search term quotation marks were used in order to find the specific phrasing of those terms. Each database search was conducted individually. One additional paper relevant to the review (Hamner et al., 1999) that had not been identified in the database search was identified in the reference list of article (Adekola et al., 2003) at the full text screening stage was included. A total of 751 articles were retrieved (PsycINFO = 331; MEDLINE = 169; WoS = 251). Of which eight studies met inclusion criteria with one additional study meeting eligibility that was not identified from the database search. Figure 1. shows a PRISMA (Preferred Reporting Items of Systematic reviews and Meta-analyses) flow diagram was used to record studies that were excluded at each stage of screening (with reasons for full text only – see Table 3. for list of reasons).

Table 3. Search terms applied to the databases

Concept 1: Psychosis (terms all combined with OR)	A N D	Concept 2: Trauma/PTSD (terms all combined with OR)	A N D	Concept 3: Ethnicity (terms all combined with OR)
exp SCHIZOPHRENIA/ exp PSYCHOSIS/ exp Psychotic Disorders/ schizo*.mp. psychos*s.mp. psychotic.mp. first episode psychos*s.mp. fep.mp. early onset psychos*s.mp. early psychos*s.mp. paranoi*.mp. delusion*.mp. hallucinat*.mp. voice*.mp. thought disorder*.mp.		exp Posttraumatic Stress Disorder/ exp Stress Disorders, Post-Traumatic/ post?traumatic stress disorder*.mp. exp trauma/ trauma.mp. ptsd.mp. adverse life event*.mp. stressful life event*.mp.		exp "racial and ethnic groups"/ exp Ethnic Groups/ ethnicity.mp. ethnicit* ethnic* group*.mp. ethnic* minorit*.mp. "minority ethnic* group*" exp REFUGEES/ refugee*.mp. race.mp. exp Ethnic Identity/
Limit to English language				
Limit to human				

Note. **PsycINFO** subject heading only; **MEDLINE** subject heading only; **Only relevant for both PsycINFO & MEDLINE**; **Keyword** term for Web of Science only

Table 4. Reason for exclusion of full text papers.

Reason for exclusion	Number
Children or Adolescent population	15
Presentation/ experiences not broken down by ethnic group	20
Did not measure psychotic disorder or symptoms	84
Trauma definition differs from review / only measured life events	15
Looked at traumatic brain injury	2
Full text not in English	4
Qualitative analysis	5
Retracted paper	1
Review article/ commentary	19
Full text version unavailable	1
Study deemed irrelevant to review ^a	52
Other reasons ^b	46

Note. ^a reasons for exclusions in this category varied but majority of papers included studies looking at disparity in healthcare/ healthcare insurance between ethnic groups or cultural diagnostic issues or were intervention studies not looking at prevalence/rates. ^b reasons for exclusions in this category were varied but typically reasons excluded were due to non-differentiation (usually in statistical analyses) of sample characteristics that were required by review specification, e.g. the population studied differed from inclusion criteria due to age of participants.

8.4 Data collection and extraction

The following variables were extracted from the studies meeting the inclusion criteria, using a standardised collection form:

- (i) primary author's name, year of publication, and study site (e.g. city or country)
- (ii) calendar date of data collection
- (iii) study design,
- (iv) type of recruitment setting (e.g. inpatient, outpatient, specialised treatment, peer, community and/or familial)
- (v) sample size
- (vi) participant characteristics (e.g. age, gender, diagnosis, population focus),
- (vii) Measurement tools used (for trauma experiences, PTSD and psychotic symptoms)
- (viii) Timing of the assessment (for trauma experiences, PTSD and psychotic symptoms)
- (ix) ethnic group studied (as defined by the study) and percentage in the sample studied/analysed
- (x) number of participants or prevalence of comorbid trauma/PTSD and psychosis by ethnic group,
- (xi) quality rating of the study, and
- (xii) additional interesting findings (e.g. moderating, confounding, modifying factors) if reported.

Within this review study the following definitions were used:

Study site: the country or city where the paper was published or from where the sample population were recruited from;

Study design: cross-sectional study – recruitment of participants in which observational data is collected from a population or subsample at a specific period of time i.e. a snapshot; case-series – recruitment of participants in which known exposure and/or outcome data is collected either consecutively or non-consecutively from a subset of population over a defined period of time.

Study/recruitment setting: as defined by the researchers

Sample size: total number of participants recruited for the study (including participants who were later excluded from analyses)

Timing of assessment: the period of time in which participants were diagnosed with the relevant disorders or experiences

8.5 Quality assessment

The quality assessment tool used in this review provides a standardised critical appraisal framework to assess the quality of the study in relation to risk of bias (see below for more details). There is a total of 14 criteria items to rate (e.g. for study population, sample size justification). Each criteria of the quality tool are judged on the basis of whether the study has adequately addressed potential for bias e.g. using the answers 'yes' or 'no' when risk of bias is

absent or present respectively. In instances where the required criteria information is unclear, unavailable or not relevant, additional ratings are used to rate the quality of that item e.g. 'CD' – cannot determine, 'NR' – not reported and 'NA' – not applicable. An overall quality rating was decided upon based on these individual ratings, with each study being rated as 'good', 'fair' or 'poor' quality rating. Quality criteria items marked CD, NR or NA will be accounted for in the rating (e.g. reflected in the overall rating for bias). Quality assessment were independently conducted by primary researcher and a second reviewer (second supervisor) and any discrepancies were discussed to reach a consensus rating. Both reviewers were not blinded to names of researchers, institutions, journals and results of the studies when assessing their methods. When assessing the quality of evidence for all studies, the 'exposure' variable was interchangeable depending on whether the primary population diagnosis was psychosis or trauma/PTSD. In instances where neither diagnosis nor experience was the primary focus of the study, the timing of assessment and the summary from the results of the study were taken into consideration in deciding this. Thus, the exposure variable was defined as either current/historical experience of trauma and/or diagnosis of PTSD or experience of psychotic symptoms/psychotic disorder diagnosis. The 'outcome' variable was therefore the inverse, with regard to which variable was considered the exposure variable. For the purpose of this review, the scale was modified as three additional items were included in the quality assessment tool in order to reflect the notable variations in the measurement of all the relevant topic concepts. Although these were not included in the final quality rating, but were used to comment on the quality of the measurement for the trauma/PTSD, psychosis and ethnicity terms. Criteria on measurement tools for psychosis and trauma/PTSD was used to reflect the varying methodology used to assess these in the literature and to capture whether diagnosis of these somewhat complex diagnoses were made by junior research assistants or senior researchers or clinicians. The additional criteria for ethnicity was added to reflect how detailed or specific ethnicity was defined as the concept can be very subjective and some studies tend to collapse ethnically diverse groups into the same category. Scores for each of these items were allocated from 0-2, with a score of 2 representing the best quality rating for that criteria. Overall quality ratings are included in Table 1 and Table 2

The quality measure is comprised of a list of criteria for assessing bias. The purpose of the list of criteria is not intended to form a simple tally before making a judgement on the quality of the study. The critical appraisal process involves the consideration of potential risk of bias that the study artefacts e.g. selection bias, measurement bias, have had an impact on the results of the study. That is, to evaluate the extent to which the exposure variable has contributed to the outcomes and findings of the study which are not attributable to flaws in the design or conduct of the study. Any of these defects contribute to an increased risk of bias.

Potential areas of bias will include selection bias (related to selection or recruitment of study sample, missing information related to time period and/or setting of study); attrition bias (incomplete outcome data or absence and/or exclusion of participants deemed unclear or not justified) and reporting bias (selective reporting, inaccurate, incomplete or unclear outcome reporting). In addition, consideration for adjustment of potential confounders will be commented on, for example, comorbidity of other disorders not included in the review, e.g. depression, demographics factors such as age, gender and so on.

8.6 Quality assessment tool

Quality Assessment Tool for Observational Cohort and Cross-sectional Studies (US Department of Health, 2013)

Author, year of publication, title:			
Checklist completed by:			
Criteria	Yes	No	Other (CD, cannot determine; NA, not applicable; NR, not reported)
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Was the participation rate of eligible persons at least 50%?			
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
5. Was a sample size justification, power description, or variance and effect estimates provided?			
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10. Was the exposure(s) assessed more than once over time?			
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
12. Were the outcome assessors blinded to the exposure status of participants?			
13. Was loss to follow-up after baseline 20% or less?			
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			
Additional criteria/score	0	1	2
How was trauma/PTSD measured? Clinician-only diagnosis or simplified checklist = 0, Interviewer administered checklist/ Structured assessment or self-report measure by trained research worker = 1, Structured interview/ assessment by clinician = 2			
How was psychosis measured? Clinician-only diagnosis or simplified checklist = 0, Structured interview/ assessment by trained research worker, or self-report measure for psychotic experiences = 1, Structured assessment by clinician = 2			
What was the quality of ethnicity measurement tool? Simplified categorisation e.g. whites, blacks, other etc. = 0, self-reported only without use of valid, standardised assessment tool and/or condensing of ethnic groups shown to have variations in variable of interest = 1, self-reported and collected use of valid, standardised assessment tool AND ethnically distinct groups (e.g. Black African and Black Caribbean not condensed)			
Additional comments:			

8.7 Guidance for assessing the quality of observational cohort and cross-sectional studies



National Heart, Lung,
and Blood Institute

Guidance for Assessing the Quality of Observational Cohort and Cross-Sectional Studies

The guidance document below is organized by question number from the tool for quality assessment of observational cohort and cross-sectional studies.

Question 1. Research question

Did the authors describe their goal in conducting this research? Is it easy to understand what they were looking to find? This issue is important for any scientific paper of any type. Higher quality scientific research explicitly defines a research question.

Questions 2 and 3. Study population

Did the authors describe the group of people from which the study participants were selected or recruited, using demographics, location, and time period? If you were to conduct this study again, would you know who to recruit, from where, and from what time period? Is the cohort population free of the outcomes of interest at the time they were recruited?

An example would be men over 40 years old with type 2 diabetes who began seeking medical care at Phoenix Good Samaritan Hospital between January 1, 1990 and December 31, 1994. In this example, the population is clearly described as: (1) who (men over 40 years old with type 2 diabetes); (2) where (Phoenix Good Samaritan Hospital); and (3) when (between January 1, 1990 and December 31, 1994). Another example is women ages 34 to 59 years of age in 1980 who were in the nursing profession and had no known coronary disease, stroke, cancer, hypercholesterolemia, or diabetes, and were recruited from the 11 most populous States, with contact information obtained from State nursing boards.

In cohort studies, it is crucial that the population at baseline is free of the outcome of interest. For example, the nurses' population above would be an appropriate group in which to study incident coronary disease. This information is usually found either in descriptions of population recruitment, definitions of variables, or inclusion/exclusion criteria.

You may need to look at prior papers on methods in order to make the assessment for this question. Those papers are usually in the reference list.

If fewer than 50% of eligible persons participated in the study, then there is concern that the study population does not adequately represent the target population. This increases the risk of bias.

Question 4. Groups recruited from the same population and uniform eligibility criteria

Were the inclusion and exclusion criteria developed prior to recruitment or selection of the study population? Were the same underlying criteria used for all of the subjects involved? This issue is related to the description of the study population, above, and you may find the information for both of these questions in the same section of the paper.

Most cohort studies begin with the selection of the cohort; participants in this cohort are then measured or evaluated to determine their exposure status. However, some cohort studies may recruit or select exposed participants in a different time or place than unexposed participants, especially retrospective cohort studies –which is when data are obtained from the past (retrospectively), but the analysis examines exposures prior to outcomes. For example, one research question could be whether diabetic men with clinical depression are at higher risk for cardiovascular disease than those without clinical depression. So, diabetic men with depression might be selected from a mental health clinic, while diabetic men without depression might be selected from an internal medicine or endocrinology clinic. This study recruits groups from different clinic populations, so this example would get a "no."

However, the women nurses described in the question above were selected based on the same inclusion/exclusion criteria, so that example would get a "yes."

Question 5. Sample size justification

Did the authors present their reasons for selecting or recruiting the number of people included or analyzed? Do they note or discuss the statistical power of the study? This question is about whether or not the study had enough participants to detect an association if one truly existed.

A paragraph in the methods section of the article may explain the sample size needed to detect a hypothesized difference in outcomes. You may also find a discussion of power in the discussion section (such as the study had 85 percent power to detect a 20 percent increase in the rate of an outcome of interest, with a 2-sided alpha of 0.05). Sometimes estimates of variance and/or estimates of effect size are given, instead of sample size calculations. In any of these cases, the answer would be "yes."

However, observational cohort studies often do not report anything about power or sample sizes because the analyses are exploratory in nature. In this case, the answer would be "no." This is not a "fatal flaw." It just may indicate that attention was not paid to whether the study was sufficiently sized to answer a prespecified question—i.e., it may have been an exploratory, hypothesis-generating study.

Question 6. Exposure assessed prior to outcome measurement

This question is important because, in order to determine whether an exposure causes an outcome, the exposure must come before the outcome.

For some prospective cohort studies, the investigator enrolls the cohort and then determines the exposure status of various members of the cohort (large epidemiological studies like Framingham used this approach). However, for other cohort studies, the cohort is selected based on its exposure status, as in the example above of depressed diabetic men (the exposure being depression). Other examples include a cohort identified by its exposure to fluoridated drinking water and then compared to a cohort living in an area without fluoridated water, or a cohort of military personnel exposed to combat in the Gulf War compared to a cohort of military personnel not deployed in a combat zone.

With either of these types of cohort studies, the cohort is followed forward in time (i.e., prospectively) to assess the outcomes that occurred in the exposed members compared to nonexposed members of the cohort. Therefore, you begin the study in the present by looking at groups that were exposed (or not) to some biological or behavioral factor, intervention, etc., and then you follow them forward in time to examine outcomes. If a cohort study is conducted

properly, the answer to this question should be "yes," since the exposure status of members of the cohort was determined at the beginning of the study before the outcomes occurred.

For retrospective cohort studies, the same principal applies. The difference is that, rather than identifying a cohort in the present and following them forward in time, the investigators go back in time (i.e., retrospectively) and select a cohort based on their exposure status in the past and then follow them forward to assess the outcomes that occurred in the exposed and nonexposed cohort members. Because in retrospective cohort studies the exposure and outcomes may have already occurred (it depends on how long they follow the cohort), it is important to make sure that the exposure preceded the outcome.

Sometimes cross-sectional studies are conducted (or cross-sectional analyses of cohort-study data), where the exposures and outcomes are measured during the same timeframe. As a result, cross-sectional analyses provide weaker evidence than regular cohort studies regarding a potential causal relationship between exposures and outcomes. For cross-sectional analyses, the answer to Question 6 should be "no."

Question 7. Sufficient timeframe to see an effect

Did the study allow enough time for a sufficient number of outcomes to occur or be observed, or enough time for an exposure to have a biological effect on an outcome? In the examples given above, if clinical depression has a biological effect on increasing risk for CVD, such an effect may take years. In the other example, if higher dietary sodium increases BP, a short timeframe may be sufficient to assess its association with BP, but a longer timeframe would be needed to examine its association with heart attacks.

The issue of timeframe is important to enable meaningful analysis of the relationships between exposures and outcomes to be conducted. This often requires at least several years, especially when looking at health outcomes, but it depends on the research question and outcomes being examined.

Cross-sectional analyses allow no time to see an effect, since the exposures and outcomes are assessed at the same time, so those would get a "no" response.

Question 8. Different levels of the exposure of interest

If the exposure can be defined as a range (examples: drug dosage, amount of physical activity, amount of sodium consumed), were multiple categories of that exposure assessed? (for example, for drugs: not on the medication, on a low dose, medium dose, high dose; for dietary sodium, higher than average U.S. consumption, lower than recommended consumption, between the two). Sometimes discrete categories of exposure are not used, but instead exposures are measured as continuous variables (for example, mg/day of dietary sodium or BP values).

In any case, studying different levels of exposure (where possible) enables investigators to assess trends or dose-response relationships between exposures and outcomes—e.g., the higher the exposure, the greater the rate of the health outcome. The presence of trends or dose-response relationships lends credibility to the hypothesis of causality between exposure and outcome.

For some exposures, however, this question may not be applicable (e.g., the exposure may be a dichotomous variable like living in a rural setting versus an urban setting, or vaccinated/not

vaccinated with a one-time vaccine). If there are only two possible exposures (yes/no), then this question should be given an "NA," and it should not count negatively towards the quality rating.

Question 9. Exposure measures and assessment

Were the exposure measures defined in detail? Were the tools or methods used to measure exposure accurate and reliable—for example, have they been validated or are they objective? This issue is important as it influences confidence in the reported exposures. When exposures are measured with less accuracy or validity, it is harder to see an association between exposure and outcome even if one exists. Also as important is whether the exposures were assessed in the same manner within groups and between groups; if not, bias may result.

For example, retrospective self-report of dietary salt intake is not as valid and reliable as prospectively using a standardized dietary log plus testing participants' urine for sodium content. Another example is measurement of BP, where there may be quite a difference between usual care, where clinicians measure BP however it is done in their practice setting (which can vary considerably), and use of trained BP assessors using standardized equipment (e.g., the same BP device which has been tested and calibrated) and a standardized protocol (e.g., patient is seated for 5 minutes with feet flat on the floor, BP is taken twice in each arm, and all four measurements are averaged). In each of these cases, the former would get a "no" and the latter a "yes."

Here is a final example that illustrates the point about why it is important to assess exposures consistently across all groups: If people with higher BP (exposed cohort) are seen by their providers more frequently than those without elevated BP (nonexposed group), it also increases the chances of detecting and documenting changes in health outcomes, including CVD-related events. Therefore, it may lead to the conclusion that higher BP leads to more CVD events. This may be true, but it could also be due to the fact that the subjects with higher BP were seen more often; thus, more CVD-related events were detected and documented simply because they had more encounters with the health care system. Thus, it could bias the results and lead to an erroneous conclusion.

Question 10. Repeated exposure assessment

Was the exposure for each person measured more than once during the course of the study period? Multiple measurements with the same result increase our confidence that the exposure status was correctly classified. Also, multiple measurements enable investigators to look at changes in exposure over time, for example, people who ate high dietary sodium throughout the followup period, compared to those who started out high then reduced their intake, compared to those who ate low sodium throughout. Once again, this may not be applicable in all cases. In many older studies, exposure was measured only at baseline. However, multiple exposure measurements do result in a stronger study design.

Question 11. Outcome measures

Were the outcomes defined in detail? Were the tools or methods for measuring outcomes accurate and reliable—for example, have they been validated or are they objective? This issue is important because it influences confidence in the validity of study results. Also important is whether the outcomes were assessed in the same manner within groups and between groups.

An example of an outcome measure that is objective, accurate, and reliable is death—the outcome measured with more accuracy than any other. But even with a measure as objective

as death, there can be differences in the accuracy and reliability of how death was assessed by the investigators. Did they base it on an autopsy report, death certificate, death registry, or report from a family member? Another example is a study of whether dietary fat intake is related to blood cholesterol level (cholesterol level being the outcome), and the cholesterol level is measured from fasting blood samples that are all sent to the same laboratory. These examples would get a "yes." An example of a "no" would be self-report by subjects that they had a heart attack, or self-report of how much they weigh (if body weight is the outcome of interest).

Similar to the example in Question 9, results may be biased if one group (e.g., people with high BP) is seen more frequently than another group (people with normal BP) because more frequent encounters with the health care system increases the chances of outcomes being detected and documented.

Question 12. Blinding of outcome assessors

Blinding means that outcome assessors did not know whether the participant was exposed or unexposed. It is also sometimes called "masking." The objective is to look for evidence in the article that the person(s) assessing the outcome(s) for the study (for example, examining medical records to determine the outcomes that occurred in the exposed and comparison groups) is masked to the exposure status of the participant. Sometimes the person measuring the exposure is the same person conducting the outcome assessment. In this case, the outcome assessor would most likely not be blinded to exposure status because they also took measurements of exposures. If so, make a note of that in the comments section.

As you assess this criterion, think about whether it is likely that the person(s) doing the outcome assessment would know (or be able to figure out) the exposure status of the study participants. If the answer is no, then blinding is adequate. An example of adequate blinding of the outcome assessors is to create a separate committee, whose members were not involved in the care of the patient and had no information about the study participants' exposure status. The committee would then be provided with copies of participants' medical records, which had been stripped of any potential exposure information or personally identifiable information. The committee would then review the records for prespecified outcomes according to the study protocol. If blinding was not possible, which is sometimes the case, mark "NA" and explain the potential for bias.

Question 13. Followup rate

Higher overall followup rates are always better than lower followup rates, even though higher rates are expected in shorter studies, whereas lower overall followup rates are often seen in studies of longer duration. Usually, an acceptable overall followup rate is considered 80 percent or more of participants whose exposures were measured at baseline. However, this is just a general guideline. For example, a 6-month cohort study examining the relationship between dietary sodium intake and BP level may have over 90 percent followup, but a 20-year cohort study examining effects of sodium intake on stroke may have only a 65 percent followup rate.

Question 14. Statistical analyses

Were key potential confounding variables measured and adjusted for, such as by statistical adjustment for baseline differences? Logistic regression or other regression methods are often used to account for the influence of variables not of interest.

This is a key issue in cohort studies, because statistical analyses need to control for potential confounders, in contrast to an RCT, where the randomization process controls for potential confounders. All key factors that may be associated both with the exposure of interest and the outcome—that are not of interest to the research question—should be controlled for in the analyses.

For example, in a study of the relationship between cardiorespiratory fitness and CVD events (heart attacks and strokes), the study should control for age, BP, blood cholesterol, and body weight, because all of these factors are associated both with low fitness and with CVD events. Well-done cohort studies control for multiple potential confounders.

Some general guidance for determining the overall quality rating of observational cohort and cross-sectional studies

The questions on the form are designed to help you focus on the key concepts for evaluating the internal validity of a study. They are not intended to create a list that you simply tally up to arrive at a summary judgment of quality.

Internal validity for cohort studies is the extent to which the results reported in the study can truly be attributed to the exposure being evaluated and not to flaws in the design or conduct of the study—in other words, the ability of the study to draw associative conclusions about the effects of the exposures being studied on outcomes. Any such flaws can increase the risk of bias.

Critical appraisal involves considering the risk of potential for selection bias, information bias, measurement bias, or confounding (the mixture of exposures that one cannot tease out from each other). Examples of confounding include co-interventions, differences at baseline in patient characteristics, and other issues throughout the questions above. High risk of bias translates to a rating of poor quality. Low risk of bias translates to a rating of good quality. (Thus, the greater the risk of bias, the lower the quality rating of the study.)

In addition, the more attention in the study design to issues that can help determine whether there is a causal relationship between the exposure and outcome, the higher quality the study. These include exposures occurring prior to outcomes, evaluation of a dose-response gradient, accuracy of measurement of both exposure and outcome, sufficient timeframe to see an effect, and appropriate control for confounding—all concepts reflected in the tool.

Generally, when you evaluate a study, you will not see a "fatal flaw," but you will find some risk of bias. By focusing on the concepts underlying the questions in the quality assessment tool, you should ask yourself about the potential for bias in the study you are critically appraising. For any box where you check "no" you should ask, "What is the potential risk of bias resulting from this flaw in study design or execution?" That is, does this factor cause you to doubt the results that are reported in the study or doubt the ability of the study to accurately assess an association between exposure and outcome?

The best approach is to think about the questions in the tool and how each one tells you something about the potential for bias in a study. The more you familiarize yourself with the key concepts, the more comfortable you will be with critical appraisal. Examples of studies rated good, fair, and poor are useful, but each study must be assessed on its own based on the details that are reported and consideration of the concepts for minimizing bias.

Empirical research project

The prevalence & correlates of first episode psychosis (FEP) and the impact of trauma and discrimination on risk of FEP.

Adanna Onyejiaka

Supervised by Professor Craig Morgan & Dr Lucia Valmaggia

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Empirical Research Project

The prevalence & correlates of first episode psychosis (FEP) and the impact of trauma and discrimination on risk of FEP.

1. Abstract

Background. Adverse environmental factors such as trauma and discrimination have been implicated in the aetiology of psychosis given the number of individuals with psychotic disorders reporting these kinds of experiences (Cantor-Graae & Selten, 2005; Fearon et al., 2006). These associations have also led to increased interest in uncovering the mechanisms involved. Cognitive models of psychosis have proposed the importance of key factors such as cognitive processes in the development and maintenance of psychotic symptoms (Garety, Kuipers, Fowler, Freeman, & Bebbington, 2001; Gracie et al., 2007). The current study aims to assess the independent influence of trauma or discrimination; and the relationship between trauma and negative schematic beliefs on the odds of psychosis.

Method. Within a case-control study (262 first episode cases and 256 population-based controls), the Harvard Trauma Questionnaire, Discrimination questionnaire and the Brief Core Schema Scales were used to assess severe lifetime trauma, experience of discrimination and presence of negative schematic beliefs, respectively. Logistic regressions were used to assess the main effects of trauma and discrimination (independently) on odds of psychosis. The mediating and moderating influence of negative schemas on the trauma and psychosis association were analysed.

Results. Trauma and discrimination were associated with increased odds of psychosis; OR 3.17 and 1.96, respectively. Negative beliefs of oneself (15%) and others (11%) partially mediated the association between trauma and psychosis. Negative beliefs of others but not of oneself moderated the relationship between trauma and psychosis by increasing odds (OR = 5.24).

Conclusion. The study reiterated previous findings highlighting the impact of trauma and discrimination on odds of psychotic disorder, and in considering the role of potential cognitive processes. The clinical implications of the findings are discussed.

2. Introduction/ Literature review

2.1 Psychosis

Psychosis is an umbrella term that is used to classify disorders such as schizophrenia, schizoaffective, schizophreniform, schizotypal and delusional disorders (American Psychiatric Association, 2013; NICE, 2014; World Health Organization, 1992). However, the concept of psychosis remains contested. Whilst the experience and symptoms of psychosis are phenomenologically observed in a subset of individuals within the general population, its conceptualisation is less clear (Cooke et al., 2014). Schizophrenia and other psychoses are generally considered to be multifaceted disorders, with many interrelated risk factors. In the last few years the conventional view that genetic and biological factors solely influence the development and maintenance of psychosis has seen some shifts. Research into the aetiology of psychosis has focused on potential psychological and social factors, and stress broadly defined is one key factor that has been consistently implicated. One expanding area is the research investigating the relationship between trauma and psychosis. Trauma, particularly chronic exposure to stressors, has been associated with increased risk of developing symptoms in both clinical and non-clinical populations.

2.2 Trauma and psychosis

There has been mounting interest in the association between a history of trauma (e.g. childhood abuse, peer bullying) and psychosis due to the significant number of individuals with psychotic disorders reporting traumatic experiences (Fearon & Morgan, 2006; Fisher et al., 2010). Read and colleagues (2005) made the declarative statement that childhood trauma can be a cause of psychosis. Given that only a small percentage of those exposed to childhood adversity go on to develop psychosis, this claim needs to be further explored. Furthermore, the literature exploring the relationship between trauma and onset of psychosis suffers from many methodological

limitations (Morgan & Fisher, 2007). Nevertheless, whilst there is not substantial evidence to support this unequivocal claim, many researchers have highlighted the role of trauma in the development and maintenance of psychosis. There are a number of non-mutually exclusive mechanisms through which childhood adversity, or more broadly trauma, may contribute to the onset of psychosis through social, psychological and biological processes. In addition, the manifestation of a psychotic disorder is dependent on individual level, interpersonal and/or and societal factors, for example coping behaviour (Rudnick & Martins, 2009). This proposed notion lends itself to the stress-vulnerability models (Nuechterlein & Dawson, 1984; Zubin & Spring, 1977) and traumagenic neurodevelopment model (John Read et al., 2014) of psychosis formation and maintenance. Other models have highlighted specific cognitive and emotional states and their implications for the aetiology of psychosis (Freeman, Garety, Kuipers, Fowler, & Bebbington, 2002; Garety et al., 2001; Kuipers et al., 2006).

2.2.1 Psychological processes, trauma and psychosis: possible mechanism

2.2.1.1 Negative schemas

In both clinical and non-clinical samples, core schematic beliefs about oneself and others have been associated with psychotic symptoms such as paranoia, delusions and hallucinations (Beck & Rector, 2003; Bentall, Corcoran, Howard, Blackwood, & Kinderman, 2001; Fowler, 2000; Freeman et al., 2012; Gracie et al., 2007; Smith et al., 2006; Thomas, Farhall, & Shawyer, 2015). Schemas are considered to be cognitive structures which are made up of core beliefs about the self, others, world and future (Beck, 1967, 1979). They are developed in the formative early years of life and considered to be relatively stable (J. E. Young, 1994). The formation of such beliefs may manifest through enduring rules and standards of living (Bentall et al., 2001). Although, these explanations were developed in relation to Beck's cognitive model of depression, they can be applied to psychosis.

In relation to the association between trauma and psychosis, some psychological models of psychosis propose that early traumatic experiences can lead to cognitive predisposition for psychosis, through the development of negative core beliefs about oneself and others which in turn may bias an individual's appraisal to view themselves, others and the world as more negative and threatening. These factors may also lead to increased affective disturbances as well as contribute to the symptoms and distress maintenance by influencing appraisals of anomalous experiences (Garety, Bebbington, Fowler, Freeman, & Kuipers, 2007; Garety et al., 2001). Cognitive schemas may be reactivated later on in life when the individual experiences further traumatic or adverse events. When activated these schemas may influence and bias the appraisals of such events i.e. the thinking patterns and interpretations inform the individuals' experience. It is these negative reasoning biases in the moment to moment processing of anomalous experiences which increase the vulnerability for onset and maintenance of psychotic symptoms (Garety et al., 2001). Thus, early traumatic experiences and further trauma in adulthood, are likely to perpetuate an enduring cognitive vulnerability, characterised by negative schematic beliefs about oneself, others and the world that serve to facilitate maladaptive reasoning biases and thus manifestation of psychosis (Garety et al., 2007; Garety et al., 2001).

Specifically, negative schemas of oneself (e.g. as worthless, bad, vulnerable) and others (e.g. as dangerous, untrustworthy), are believed to be implicated in the underlying themes of threat and suspiciousness in paranoid and delusional thoughts (Freeman et al., 2002). This finding has also been demonstrated in non-clinical samples. Fowler and colleagues (2006) found that paranoia was associated with negative beliefs about oneself and others in a general population of students. Negative schemas are also thought to increase risk of psychosis through biased appraisals of anomalous experiences and exerting influence on increasing negative affect (Freeman et al., 2002; Garety et al., 2007).

The association between adverse experiences (e.g. lifetime stressors, childhood trauma) and psychotic symptoms have been shown to be mediated by core beliefs (Fisher, Appiah-Kusi, & Grant, 2012; Freeman et al., 2012; Freeman et al., 2014; Sündermann, Onwumere, Kane, Morgan, & Kuipers, 2014). For example, the relationship between childhood emotional and psychological abuse and paranoia in adulthood was partially mediated by negative self beliefs and anxiety (Fisher et al., 2012).

Thus, it is plausible that trauma could interact with cognitive mechanisms underlying psychotic symptoms, whereby stress re-activates latent cognitive beliefs (and affective changes) in vulnerable individuals (i.e. predisposing biopsychosocial factors), that lead to an anomalous experience (e.g. hallucination), which then lead to biased appraisals of this experience (Garety & Freeman, 2013; Garety et al., 2007). It is these biased appraisals, rather than just the experience of anomaly, that are important in the development and maintenance of psychosis (Garety et al., 2007; Garety et al., 2001).

2.3 Social adversity and psychosis

The literature on the impact of social adversity, broadly defined, on the aetiology and maintenance of psychosis is also emerging and being recognised as potentially important (Cantor-Graae & Selten, 2005; Garety et al., 2001; Morgan et al., 2009; Morgan et al., 2008). Experiences of social adversity, as with traumatic events, could influence cognitive and affective processes that manifest as psychotic symptoms. In psychosis research, the tendency is towards investigating fairly crude proxies of social adversity such as migration, urbanicity and ethnicity that can be difficult to interpret (March, Morgan, Bresnahan, & Susser, 2008). In addition, given the reliance on retrospective studies in looking at the relationship between makers of social adversity and psychosis, causal directions cannot be determined. The functional decline that occurs for many with a psychotic disorder increases this difficulty even further. Whilst it has

been demonstrated that migration, urbanicity and ethnicity are associated with heightened risk of psychosis (Bhavsar, Boydell, Murray, & Power, 2014; Boydell et al., 2001; Kirkbride, Jones, Ullrich, & Coid, 2012), the mechanisms through which these exert their effects on risk of psychosis is less clear, as exposure to these experiences are likely to be complex, cumulative and contribute in varying ways between individuals (van Os, Kenis, & Rutten, 2010). In addition, migration, urbanicity and ethnicity are often interlinked, making their inter-relationships difficult to disentangle. One potential common factor which links the exposure to these stressors with psychosis is the experience of perceived racial and other discrimination that may emerge from these. For example, the process of migration may leave an individual exposed to the experience of racism and discrimination which may explain some of the relationship between ethnicity and psychosis. Furthermore, urbanicity may be associated with difficulties such as increased victimisation, poor social housing and socio-economic status that may be perceived as discrimination by the individual. Such effects of broad social markers with individual level factors on psychosis risk have been highlighted in the literature. For example, Cooper and colleagues (2008) found that the relationship between markers of social adversity and psychosis were mediated by perceptions of disadvantage. This demonstrates how environmental level factors (e.g. experience of adversity) may be compounded by the individual's perception of such experiences (Allardyce & Boydell, 2006). The converse of this relationship has also been highlighted; for example, Becares and colleagues (2009) showed that the effect of ethnic discrimination was buffered by ethnic density of the area.

2.3.1 A key role for discrimination?

Racial and/or ethnic discrimination (terms used interchangeably), in particular, has been associated with negative psychological outcomes such as anxiety, depression, emotional reactivity and lowered self-esteem (Carter, 2007; Mossakowski, 2003; Williams, Neighbors, & Jackson, 2003). Although the effects of racial discrimination are acknowledged and researched

in relation to mental health, they do not tend to investigate the direct effects of racism and when race-related stress has been studied, trauma is not considered as a possible reaction (Carter, 2007). Pieterse and colleagues (2010) sought to investigate putative associations between ethnic discrimination and trauma-related symptoms. They found in their sample of racially diverse college undergraduates that when controlling for generic life stress, perceived ethnic discrimination contributed to an additional 10% and 7% of variance in trauma-related symptoms for Black and Asian students, respectively. Nevertheless, it is important to state the current criteria for trauma/PTSD excludes experiences of discrimination. However, ethnic discrimination are considered to be a particular type of life stressor (Pieterse et al., 2010).

In relation to psychosis research, studies which look at racial and/or ethnic discrimination tend to focus instead on approximations or manifestations of racial discrimination such as low economic status or effects of migration. It has been replicated in a number of studies that the relative incidence of psychosis among migrants increases as they form a decreasing proportion of the population (Boydell et al., 2001; Kirkbride et al., 2007; Veling et al., 2008). The findings have been suggested to underlie the detrimental effects of exposure to discrimination in isolated migrants and potential protective effect of social support in high ethnic density neighbourhoods (Bourque et al., 2011). Experience of discrimination may also be implicated in psychosis through its influence on and interplay with biopsychosocial processes that lead to manifestation of psychotic symptoms. Selten and Cantor-Graae (2005) proposed that chronic experiences of discrimination can lead to dopaminergic hyperactivity in the mesocorticolimbic system increasing the risk of the manifestation of psychosis. Furthermore, perceived discrimination was shown to be a predictor for the development of delusional ideation (Janssen et al., 2003). The direct relation between discrimination and psychosis is in line with current psychological models of psychosis (Fowler et al., 2006; Garety et al., 2007).

Given the high rates of psychosis in ethnic minority groups, it would seem plausible that the experience of discrimination could be implicated in the aetiology of psychosis. Veling and colleagues (2007) showed that discrimination perceived by migrants rather than social factors related to adjustments in the host country contributed to the ethnic minority groups' increased risk of schizophrenia. Others have added to the evidence by reporting dose-response relationship between discrimination and severity of psychotic symptoms (Veling, 2013; Veling et al., 2008). Indeed, the greater persistence of inequalities in social adverse experiences in non-White groups than in their White counterparts has been attributed to racial discrimination and experiences of racism, which may in turn increase predisposition to psychosis (Janssen et al., 2003; Karlsen & Nazroo, 2002; Selten & Cantor-Graae, 2005). Additionally, it has been suggested that ethnic minorities may have more adverse reactions to, or perceptions of adversity that increases their vulnerability to psychosis (as highlighted in (C. Cooper et al., 2008) above). Furthermore, Gilvarry and colleagues (1999) reported that Black African and Black Caribbean psychosis samples were more likely to attribute adverse experiences to discriminatory behaviour rather than chance compared to other ethnic groups. Whilst Berg and colleagues (2011) found that perceived discrimination correlated with psychotic symptoms ($r = 0.26$, $p < 0.05$) and partially mediated symptom severity in the African migrants. Additionally, evidence for the potential role of ethnic discrimination have been demonstrated in subclinical psychosis populations. Shaikh and colleagues (2016) found in their sample of ultra-high risk for psychosis individuals that perceived ethnic discrimination was positively correlated with persecutory paranoia ($r = 0.12$, $p < 0.01$). Whilst Oh and colleagues (2014) demonstrated in the ethnically diverse sample that perceived discrimination was associated with both 12-month psychotic experiences (adj. OR = 4.59, $p < 0.01$) and lifetime psychotic experiences (adj. OR = 3.75, $p < 0.01$). The evidence seems to suggest that individuals from Black and Minority Ethnic (BME) groups may be more vulnerable to developing psychosis following exposure to adversity and/or due to perception of these experiences.

2.4 Ethnicity and Psychosis

As highlighted above, the literature has consistently evidenced that the incidence of schizophrenia and other psychoses is higher in migrant and minority ethnic groups, and there is some evidence implicating exposure to high levels of social adversity, crudely defined (Morgan, Charalambides, Hutchinson, & Murray, 2010). The Aetiology and Ethnicity in Schizophrenia and Other Psychoses (AESOP) study group has highlighted the disproportionate rates of first episode psychosis in certain ethnic groups such as Black Caribbeans and Black Africans in the UK (Fearon et al., 2006). In the Netherlands, individuals of Dutch-Antillean, Surinamese and Moroccan descent have been shown to have elevated rates of psychosis in comparisons to those of Dutch native backgrounds (Selten et al., 2001). Similar findings have been demonstrated from many other countries in relation to disproportionate rates of psychosis within various ethnic groups (Bresnahan et al., 2007; Cantor-Graae, Zolkowska, & McNeil, 2005). These results require further investigation to pinpoint the factors to which these populations are exposed that has led to an overinflated risk of developing psychosis. However, the research to date, largely relies on crude indicators of adversity; data on specific individual-level exposures, such as discrimination and trauma remain sparse. In addition, there is a dearth in literature on mediating mechanisms, such as stress responsivity, cognitive schema and affective processes (i.e., development of depression and anxiety), through which such exposures may increase risk of psychotic disorder in certain groups. By comprehensively investigating the specific factors that increase population rates of psychosis in migrant and minority ethnic groups we may gain a better understanding both of the causes of psychosis in general and of potential targets for prevention and intervention.

2.5 Rationale for study

As such, there are compelling arguments to consider discrimination and trauma as strong candidate factors in understanding the elevated rates of psychosis in migrant and minority ethnic groups. Both of these factors are more prevalent in these populations, including

experiences of trauma among migrants fleeing persecution and war, and there is general evidence suggesting trauma and stress may be important in the onset of psychosis (Morgan & Fisher, 2007). It is plausible, moreover, that chronic exposure to threatening events and contexts in these groups impacts on risk through consequent increased sensitivity to stress and the development of negative views of self and of others. These possibilities, however, have not been directly tested. In relation to discrimination, whilst the influence on psychosis is implied by the current literature, this tends not be directly tested.

Greater understanding of the aetiology of psychosis could have huge implications in NHS prevention and intervention programmes for individuals suffering a first episode by providing a greater understanding of the wider context in which an individual's distress may be situated which may not reflect the Western notions of psychiatric disorder. The conceptualisation of an individual's response to traumatic events may be best understood by their cultural idioms and obtaining a greater appreciation of those concepts could be utilised in modifying treatments that address the impact of response to traumatic events.

This proposed project is of considerable public health significance. Migration, both between and within countries, continues to rise and is the primary driver behind increasing ethnic and cultural diversity in many countries (Castles, De Haas, & Miller, 2013). As indicated above, within some inner-city areas in the UK (notably London) individuals from migrant and minority ethnic groups now form a majority of patients presenting to mental health services with a first episode of psychosis, in large part because of the high rates of disorder in these populations (Fearon et al., 2006; Morgan et al., 2006). This is arguably the most pressing challenge facing mental health services in inner city areas. It is only by more fully understanding the factors that give rise to the high rates of disorder in these groups that services will be able to meet the complex needs of increasingly diverse populations. There is, then, considerable potential impact of this project, both in terms of our understanding of how trauma and discrimination impact on risk of disorder (and therefore of the aetiology of psychosis

in general) and in informing the development of services and practice to meet the needs of migrant and minority ethnic groups.

In reviewing the literature, most of the research investigating the relationship between trauma and psychosis has focussed on the subtypes of traumatic experience in childhood on the risk of psychosis more generally (Carr, Martins, Stingel, Lemgruber, & Jurueña, 2013; Mauritz et al., 2013; Mueser et al., 1998) at the expense of investigating trauma across the lifespan. Whilst others have looked at association of trauma and psychosis which are likely to include long-standing and First Episode of Psychosis samples. However, it is important to make this distinction between these samples as chronicity may be confounded by other factors which adds to the heterogeneity of this population and to consider experiences across the lifespan. Other literature has focused specifically on the experience of refugees (Fazel et al., 2005; Parrett & Mason, 2010), which may perhaps overlook the experience of ethnic minority and migrant populations more generally.

Literature investigating the aetiology and mechanisms involved in psychosis is progressively moving towards assessing complex causal pathways through direct effects as well as using mediation and interaction (moderation) (Morgan, Reininghaus, Fearon, et al., 2014). Additionally, investigating beyond putative individual factors is important to consider given the complex impact of social context on psychosis. Thus, the proposed project can add to the widening literature, which is becoming more focused on the study of first episode psychosis and its aetiology.

2.6 Objectives, Aims and Hypotheses of the study

The main objectives of the work presented in this study were to explore the associations between severe lifetime trauma and perceived discrimination (independently) on the risk of early-onset psychosis in an ethnically diverse cohort with a psychotic disorder at their first presentation to services compared to the general population of controls recruited from the same catchment area. Given the ethnic diversity within the samples, associations of these

effects were also explored in relation to ethnicity. In addition, the study aimed to explore whether potential psychological pathways of negative schematic beliefs (of oneself and others) mediated and/or moderated the association with trauma to increase odds of psychosis of those exposed to traumatic experiences.

The research aims were as follows:

Main effects:

1. To assess whether the odds of psychosis will be greater in those who experience a) trauma and b) discrimination;
2. To assess whether the above associations vary by ethnicity.

Mediation:

3. To separately assess whether the association between psychosis and trauma is mediated by negative beliefs of oneself or others.

Moderation:

4. To separately assess whether negative schematic beliefs of oneself or others modify the association between psychosis and trauma

In relation to the above aims the following hypotheses were tested:

Main effects:

1. Experience of a) trauma and b) discrimination will be associated with increased odds of psychosis, independent of *a priori* confounders of age, gender, ethnicity and social class;
2. The odds of psychosis in relation to the above associations will be greatest in those from minority ethnic backgrounds.

Mediation:

3. The association between trauma and psychosis will be mediated by the presence of negative beliefs of a) oneself or b) others to increase the odds of psychosis.

Moderation:

4. The association between trauma and psychosis will be modified by the presence of negative beliefs of a) oneself or b) others, such that the presence of either belief will increase the odds of psychosis.

3. Method

3.1 Background and design

The data used for analyses were drawn from the Childhood Adversity and Psychosis (CAPsy) study, which is a large cross-sectional, epidemiological and case-control research project focused on incidence of First Episode Psychosis (FEP) funded by the Wellcome Trust. The study was designed to investigate the relationship between various forms of trauma and adversity and psychosis, and potential biopsychosocial mechanisms. The CAPsy study overlaps with and contributes to the European Network of National Schizophrenia Networks Studying Gene-Environmental Interactions (EU-GEI) programme of research that is investigating gene and environmental interactions in schizophrenia by focusing on first episode patients (Van Os, Rutten, & Poulton, 2008).

3.2 Ethical issues

Ethical approval for the study was obtained from the Institute of Psychiatry Psychology Neuroscience (IOPPN) and South London and Maudsley (SLAM) NHS Foundation Trust ethics committee (Ethics Reference: 321/05, including amendments 1 to 9). Informed consent was sought from all participants and they were made aware of the voluntary nature of participation

and their right to withdraw at any time. Confidentiality of assessment data was strictly maintained with the use of unique study generated identification numbers in the assessment booklets and databases. Database and computer files with identifiable information and assessment data were password protected and encrypted. Paper copies of data collected were stored in locked cabinets in a locked private office that was only accessible by a small number of researchers involved in the study. Participants were informed of the limits to confidentiality, whereby confidentiality would be breached in circumstances that were considered to put the participants or others at risk. In such circumstances, the principle investigator was consulted and a clinician relevant for the participant (e.g. GP or secondary mental health professional) was contacted.

3.3 Sample recruitment

Using a case-control design, the study recruited a sample of 332 individuals with a First Episode of Psychosis (FEP cases) and 301 population-based controls (with no history of psychosis) from the same catchment area as cases. Recruitment of participants spanned a period of approximately four years from January 2010 – January 2014 (controls were recruited over a period of three years, commencing a year after case recruitment). The scope of this present study only covers a subsample of participants who completed the key measures required for the aims of this project (i.e. completed the Harvard Trauma Questionnaire and the discrimination questionnaire).

The sample of cases were recruited from adults who presented to inpatient and outpatient services in Lambeth, Southwark and Croydon boroughs of the SLAM NHS Foundation Trust, and were experiencing their first contact with services for psychotic symptoms. Thus, they were epidemiologically characterised as a cohort of new cases of psychosis. Cases:

- a. were aged between 18 – 64 (inclusive) years of age;

- b. did not have a previous contact with secondary mental health services (e.g. inpatient units, outpatient units, community mental health teams, assertive outreach teams) for psychotic symptoms (with non-organic cause and not precipitated by acute intoxication) prior to 1st of January 2010; and
- c. were fluent in the English language (i.e. did not need an interpreter).
- d. with learning difficulties i.e. IQ less than 70 were excluded.

Controls were population-based volunteers, recruited through two methods:

- a. Postal Address File (PAF; method described by (R Jenkins & Meltzer, 1995) – via a random sample of addresses contacted by letter or home visit, using publically available list of all private households in the catchment area. Target addresses were visited by researchers on three separate occasions at different times of the day and week (unless contact was made in earlier visits) to minimise sampling bias and maximise likelihood of contact. Once contact was established with interested and eligible volunteers, participants were screened for psychosis using a self-report measure;
- b. GP services – using a random sample of individuals on case lists of GP practices contacted via letter. Clinical codes were used to exclude individuals who had a history of psychotic disorder.

Controls:

- a. were aged between 18 – 64 (inclusive) years of age;
- b. had no evidence of past or current psychotic disorders as screened by the Psychosis Screening Questionnaire (PSQ; (Bebbington & Nayani, 1995);
- c. were included if they had experienced or were currently experiencing symptoms of mental illness other than psychosis
- d. were fluent in the English language (i.e. did not need an interpreter); and

- e. were not included if there was evidence of learning impairment i.e. IQ less than 70.

A quota sampling technique was used to recruit the control participants to ensure that the sample closely resembled the characteristics of the catchment area population (in line with recent Census 2011 data; Office of National Statistics 2011) as well as the case sample (e.g. oversampling younger, “Black” ethnic controls to better reflect the number of case samples in this category who present with psychosis). Particular attention was paid to make sure the sample was as ethnically diverse and representative of the local population.

3.4 Data collection

Cases were identified by members of the research team through regular screening and checking of all points of contact with secondary and tertiary mental health services within the defined area. All those meeting the inclusion criteria were approached and informed consent sought.

For those who provided consent, meetings were arranged with cases in order to complete the assessment as soon as was feasible e.g. when not acutely psychotic or when capacity not deemed to be compromised. An extensive battery of assessments was conducted with cases, taking an average of six hours to complete (approximately over three appointments). The setting in which the assessments were carried out were determined by the particular circumstances and preference for the case. Therefore, interviews were carried out in a variety of settings, for example, on inpatient units, CMHT, home visits as well as at the IOPPN facilities.

Meetings were arranged with controls who were seen on two to three separate occasions (on average two hours each). Control participants were assessed at the IOPPN facilities or a location of their choosing that was more convenient (e.g. at home). Timing of appointments varied and arrangement to accommodate participants in full time work were applied, such as conducting evening and weekend interview slots.

Written informed consent was obtained from all eligible participants. Participants who agreed to take part in the study signed a consent form (see Appendix 7.1) and the aims, potential risks, the nature of the study as well as confidentiality issues were explained to them. Participants were reimbursed up to £30 for their involvement in the study, and were free to withdraw at any time. Given the sensitive nature of the project, participants were reminded throughout the course of interviews that they did not have to respond to questions they were uncomfortable with or did not wish to answer. All interviews of cases and controls were conducted by trained Research Workers, PhD students with a background in psychology or psychiatry and psychiatrists.

3.5 Measures

The assessments comprised a number of structured, semi-structured interviews and self-report questionnaires that were used to collect data from participants. For some individuals who found it difficult to complete the self-report measures, these were read out to the participants, with use of probes for obtaining more information. The wider study included an extensive battery of assessments which included diagnostic instruments, neuropsychological testing, biological, psychological, and social components. Only the measures relevant for this specific study are detailed in this report.

A structured proforma was used to collect data on sociodemographic characteristics. All the measures were grouped in booklets (see Appendix 7.2) with priority given to key assessments. The specific assessments relevant for this study are described in detail below:

1. Amended version of the Medical Research Council (MRC) Sociodemographic schedule (R Mallett, 1997). This includes details about sociodemographic data such as age; gender; ethnicity; country of birth (and migration status where applicable); years in education; socioeconomic status; and information on historic and current relationship

status, housing and employment. Indicators of social disadvantage can be obtained from some of this data. See Appendix 7.2 for more details. The variables relevant for the analyses of this study were gender, age, ethnicity and social class (participant's main status).

2. Harvard Trauma Questionnaire (HTQ; (R. F. Mollica et al., 1992). The HTQ is a self-report questionnaire which includes a checklist of traumatic events that are either experienced, witnessed, heard about or not experienced. Lifetime exposure to trauma was measured using the HTQ. This questionnaire was administered as a brief interview and rated positive only if the descriptions of event was deemed to be objectively meet criteria for severe trauma. The HTQ has been widely translated and used with a variety of diverse cultural groups (Cardozo, Bilukha, et al., 2004; de Fouchier et al., 2012; Jakobsen, Demott, & Heir, 2014; R. Mollica, McInnes, Sarajlić, Lavelle, & Sarajlić, 1999; Shoeb, Weinstein, & Mollica, 2007); validated against clinical diagnosis (Fawzi et al., 1997; R. F. Mollica et al., 1993) and has demonstrated high internal consistency reliability in a number of studies (Kleijn, Hovens, & Rodenburg, 2001). The HTQ was included in the battery of assessments of participants at a later time point in the recruitment period, thus participants who were recruited earlier did not complete this measure. For the purpose of this study, only traumas that were directly experienced by the participants were used in the analysis. This is in line with other previous studies which have used HTQ (Cardozo, Talley, Burton, & Crawford, 2004; R. F. Mollica et al., 1993).
3. Discrimination was assessed using a 12-item questionnaire (adapted version) (developed and validated by Williams and colleagues; Kessler, Mickelson, & Williams, 1999; Shariff-Marco et al., 2011; Williams & Neighbors, 2001; Williams, Yu, Jackson, & Anderson, 1997). This measure assessed the participant's perceived discrimination of themselves throughout their lifetime. There were 12 statements asking participants if

they felt they have ever been discriminated against in a number of different scenarios (e.g. for any reason have you ever been unfairly fired). If this question was answered positively, they were then asked the number of time this had occurred in their life, age at first occurrence, and to choose the main reason for this e.g. due to gender, race/ethnicity, religion, mental illness, sexuality, age, or specify other reason. The questions in this measure was developed based largely on results from previous qualitative studies (Essed, 1991; Feagin, 1991) and the questionnaire has demonstrated high Cronbach's alpha of 0.88 (Williams et al., 1997). The internal consistency of this measure have been validated cross-culturally with many different ethnic groups (Williams et al., 2008). This questionnaire also has some additional strengths in that it follows an explicit theoretical framework; at least 75% of its construct validity have been confirmed; and the conceptual dimensional structure is supported by evidence from factor analyses (Bastos, Celeste, Faerstein, & Barros, 2010). For the purpose of this study, the researchers administered the discrimination questionnaire in a semi-structured interview format and ambiguous answers were clarified with participants or through consensus with other research members. For the purpose of the analyses in this present study only the number of events and main reason were used. Following prior research, the total number of events (0 vs 1 or more) and the reason for perceived discrimination (racial/ethnic vs other reasons) were dichotomous variables (Borrell, Kiefe, Williams, Diez-Roux, & Gordon-Larsen, 2006; Williams et al., 2003).

4. Brief Core Schema Scale (BCCS; (Fowler et al., 2006) is a self-report questionnaire containing a list of 24 statements regarding beliefs about oneself and others. Items are assessed on a five-point rating scale (0-4). Participants were asked if they held the belief or not in a Yes/No format, and if they answered positively, the strength of their belief was rated from 1 to 4: corresponding to 1 – “believe it slightly”; 2 – “moderately”, 3 – “very much” and 4 – “believe it totally”. If answered negatively it was scored as ‘0’. Four

dimensions were generated: negative-self, positive-self, negative-others, and positive-others; all containing six items each with a possible total score range of 0-24. For the purpose of this study, only the negative-self and negative-others subscales were used in the analysis. The BCSS has been reported to be a more reliable construct for assessing individuals' beliefs about the self and other people than traditionally used self-esteem measures and more independent of mood (Fowler et al., 2006). The BCSS is considered to be a useful measure of schema in psychosis and has been shown to have good psychometric properties over a variety of constructs (Fowler et al., 2006). The internal consistency of all four schema subscales is reported to be high for both clinical and non-clinical samples. In clinical samples, the following Cronbach's alpha coefficients have been demonstrated: negative self schema (0.84) and negative other schema (0.87) (Fowler et al., 2006). The test-retest reliability of the BCSS has been shown to be stable with the following person's r reported: negative self ($r = 0.84$) and negative other ($r = 0.70$). Studies using the BCSS have found associations between negative appraisals of self and others and psychotic symptomology, particularly delusional thinking, in both clinical and non-clinical populations (Fowler et al., 2006; Freeman et al., 2012; Freeman & Garety, 2014; Gracie et al., 2007; Smith et al., 2006; Thomas et al., 2015) and this trait has been shown to be sensitive enough to differentiate between patients and controls (Fowler et al., 2006).

5. The Psychosis Screening Questionnaire (PSQ; (Bebbington & Nayani, 1995) was used to screen controls to exclude presence of current or past psychotic symptoms. The measure was administered as an interview with probes to clarify individual's responses. The PSQ is divided into five domains on hypomania, thought insertion, hallucinations, paranoia and strange experiences. Each domain has a key screening question as well as additional secondary items to establish the presence and quality of psychotic experiences (i.e. endorsement of one or more secondary probes). The PSQ has been

validated in two national surveys in the UK (Nazroo, 1997; Singleton, Lee, & Meltzer, 2002) and across different ethnic groups (Johns et al., 2004; King et al., 2005; Morgan et al., 2009). In line with previous studies, items related to hypomania were discarded (Morgan, Reininghaus, Reichenberg, et al., 2014) and items included in full in which the interviewer continued through all five domains i.e. not discontinued as soon as participant screened positive on any of the five domains (Das-Munshi et al., 2012; Rachel Jenkins et al., 2012; Morgan et al., 2009).

3.5.1 Definition of first episode psychosis for this study

Conceptualisation of first episode psychosis was defined as individuals presenting with evidence of psychotic symptoms (assessed by consensus in the research team), regardless of whether they received specific diagnoses, for the first time to psychiatric services. Individuals were recruited in line with the Screening Schedule for Psychosis (Jablensky et al., 1992). Specifically, cases were included in the study if they fulfilled either criteria C or D from the Screening Schedule for Psychosis (Jablensky et al., 1992); and symptoms were present for at least one day duration, with no evidence of organic cause.

3.5.2 Definition of ethnicity

Data on ethnicity was collated from the MRC Sociodemographic schedule. Ethnicity was documented from participants' self-ascribed description (based on 2011 Census categories), collected as part of the MRC Social Demographic Schedule (clinical notes and/or medical staff were consulted if the question was not completed). Ethnic groups were then regrouped from 18 specific ethnicity categorisations to six broader categories: White British; White Other (e.g. Irish); Black African; Black Caribbean; Asian (e.g. Indian, Bangladeshi, Pakistani); and Other (e.g. Chinese, mixed groups, other). The latter groupings were used in the analyses for this study, and the other category was used to collapse smaller ethnic groups.

3.5.3 Social class categorisation

The participants' social class were rated for two time periods: main and current using the European Socio-Economic Classification system (ESeC). The ESeC comprises of ten classes to rate social class occupations: (i) large employers, higher grade professional, administrative and managerial; (ii) lower grade professional, administrative and managerial; (iii) intermediate; (iv) small employer and self-employed (excluding agriculture); (v) self-employed; (vi) lower supervisory and lower technician; (vii) lower services, sales and clerical; (viii) lower technical; (ix) routine; (x) never worked and long-term unemployed (duration of six months or more). Additional codes were used for full-time student (xi), and non-classifiable (xii) which included economically inactive individuals e.g. carers, housewives, retirees, and unknown occupations that did not fit the other categories. For the purpose of this study, main social class was used and the categories were condensed into a six-class model as follows: 'Salaried' (i, ii), 'Intermediate' (iii, iv, v, vi), 'Working Class' (vii, viii, ix), 'Never worked or long-term unemployed' (x), 'Student (xi) and non-classifiable (xii). For this current study, there were no non-classifiable occupations, so this category was omitted from the analysis. The main social class of participants were used as confounders when adjusting for associations in the regression analyses.

3.6 Statistical analysis

Statistical analyses of the data for this study were conducted using Stata Version 14 (Stata, 2015). The scope of this study and analyses only covers a subsample of participants who completed the relevant measures required for analyses. As completion of measures varied due to attrition or non-completion, the sample size for each analysis varied as complete data analyses were conducted (core sample size for main analyses: HTQ, n = 427; Discrimination questionnaire, n = 518).

Data was initially scrutinised by cleaning database and checking for normality and skewness of continuous data (using histograms and kurtosis) and then, if needed, converted to binary variables following this inspection (further explanation of analysis strategy included in Appendix 7.3). For traumatic experiences, a two level category variable was created for analyses (e.g. 0 being no trauma and 1 representing one or more severe trauma). For discrimination, the analyses looked at the number of different types of perceived discriminatory events in the lifetime (elicited in yes or no format; dichotomised into binary variable: 0 representing no events and 1 for one or more types of events) and whether the main reason for being discriminated against was due to race or other reasons (binary variable: ethnic vs other reasons).

Descriptive analysis such as the chi-square (χ^2) test were used to compare cases and controls on key sociodemographic information. Independent samples t-tests were used to compare the difference in means between the two groups on continuous data such as age.

Logistic regression analyses were used to estimate the odd ratios (OR) for experience of a) severe lifetime trauma or b) discrimination with case-control status as main outcome, conducted both unadjusted and adjusted (adj.) for *a priori* confounders (age, gender, ethnicity and main social class). Associations are presented as OR, 95% confidence intervals (CI) and p-values. The 'mholdds' command was used in STATA to calculate odds ratios across the strata of ethnicity i.e. to address the question of whether the association between trauma and psychosis risk are the same over the strata of a third variable, in this case ethnicity. Thus, the mholdds command estimates the disease and exposure (psychosis and trauma) odds ratio for each level of the stratifying variable (ethnic groups), and tests whether the odds ratio is equal to one. A significance test of homogeneity at p-value < 0.05 was used as indication of variation by ethnicity (represented with χ^2 and p-value) (i.e., moderation [effect modification]).

Following these analyses, the mediating and moderating influence of negative core beliefs of a) oneself or b) others, was used to look at the relationship between trauma experience and case-

control status. Mediation analyses were used to assess the effect of one independent variable (X) e.g. experience of trauma, on a dependent variable (Y) i.e. case-control status, via a third variable (M), the mediator (in this case core beliefs; see Figure 1.). Brief core schema variables were categorised as a binary variable (score of 0 = absent vs score of ≥ 1 = present). The binary mediation command ('binary_mediation') was used in Stata to conduct this analysis (this uses the product of coefficients approach; (Kenny, 2008; MacKinnon & Dwyer, 1993). In line with Preacher & Hayes (Preacher & Hayes, 2008), estimates of total effects of trauma on case-control status was parsed into direct and indirect (mediation) effect. The direct effect is the influence of trauma on psychosis when controlling for negative schemas. Indirect refers to the mediating effect i.e. the effect of trauma on case-control status through the pathways of negative core beliefs (separate analyses conducted for self and other beliefs). Standardised coefficients are reported for indirect effects of core schemas, the direct effects and the total effects. Robust standard errors and 95% confidence intervals were calculated using the bootstrap command with 500 bootstrap replications.

Moderation analysis was used to assess the interaction between trauma experience and negative core beliefs (self and others) on the odds of psychosis using a likelihood ratio test ('lrtest' command in Stata) to compare models with and without the interaction term. That is, to test whether the association between trauma and case-control status varies by another variable – negative core schemas (see Figure 2.). Logistic regression was used to analyse the association between trauma as the exposure variable and status i.e. case-control as outcome for use in subsequent models. This was done firstly with the whole sample then with an interaction term fitted for absence or presence of negative schemas*trauma and without the interaction term. The likelihood ratio tests were then used to assess interactions on a multiplicative scale for each negative schema (self or other) on the association between trauma

and case-control status to evaluate presence of effect modification. The significance level i.e. p-value of this analysis was used to assess presence of moderation effect at the level $p < 0.05$.

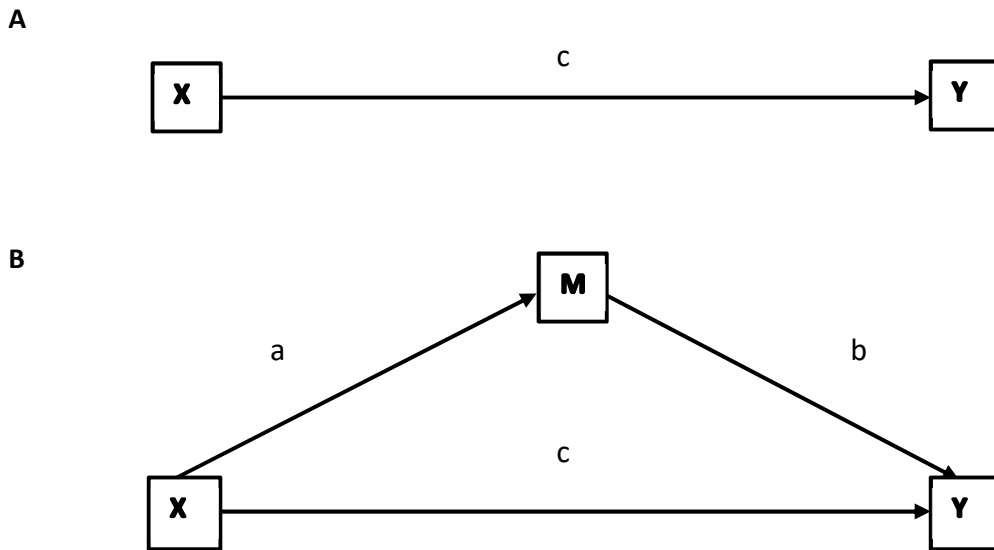


Figure 1. Illustration of a simple mediation model. A represents a direct main effect. B represents a mediation model, M is a variable said to mediate the effect of X on Y.

Note. **Direct effect (DE)** of X on Y: is the effect along the direct link between X and Y. In the figure this effect is caught by the parameter c (i.e., $DE = c$)

Indirect effect (IE) of X on Y: is the effect along indirect link between X and Y. in the figure this effect is $IE = (a \times b)$

Total Effect (TE) of X on Y: is the sum of the direct and indirect effect, i.e. $TE = DE + IE = c + (a \times b)$

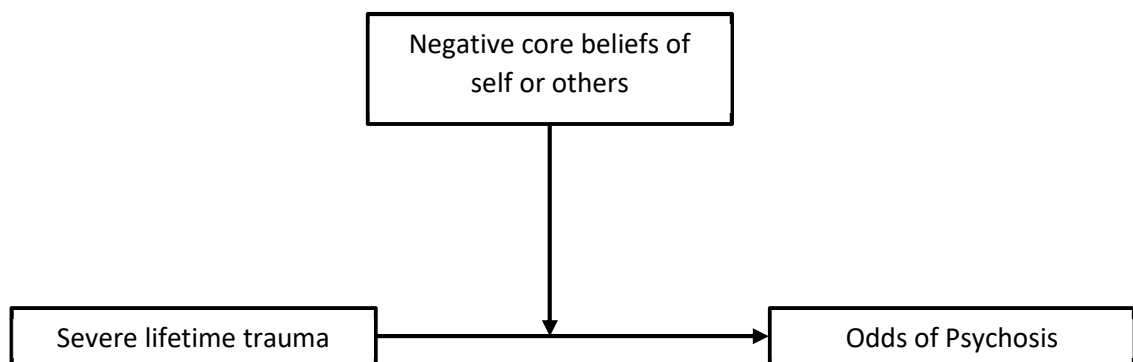


Figure 2. Diagram demonstrating effect modification model.

Note. The effect of the exposure variable (severe lifetime trauma) depends on another variable (negative core beliefs) to increase odds of psychosis.

3.6.1 Power

A post-hoc power analysis was performed using G* Power (Faul, Erdfelder, Buchner, & Lang, 2009) for the main analyses for trauma in which 204 cases and 223 controls (total sample 427) completed the HTQ. Conservatively assuming a prevalence of exposure to lifetime severe trauma of 0.30 in cases and 0.15 in controls, it was calculated that the sample size would have over 95% power to detect what is a difference in proportions of 0.15 (i.e., an OR of 2.4). With a sample of 400, using a conservative rule allowing for one parameter for every 20 participants, this would allow up to 20 variables to be entered into regression, interaction and mediation models. As the final sample (for the completed relevant measures) exceeded this, the sample size appears justified for these analyses.

4. Results

4.1 Participant demographics and descriptive analysis

The total sample of cases in the wider study was 332 and of controls was 301. Table 1 shows the basic descriptive analysis between cases and controls recruited into the study. As expected, cases were younger (mean age 29 in cases vs 35 in controls; $t = 7.25$; $df\ 631$; $p < 0.01$), more likely to be male (61.75% vs 50.83%; $\chi^2 = 7.66$; $df\ 1$, $p = 0.006$), belong to a lower social class ($p < 0.01$) and of non-White ethnicity ($p < 0.01$) than controls.

Table 1: Basic demographic of psychosis cases and controls

Demographic variable	Cases (n = 332)	Controls (n = 301)	χ^2	Df	p
	n (%)	n (%)			
Sex			7.66	1	< 0.01
Male	205 (61.75)	153 (50.83)			
Female	127 (38.25)	148 (49.17)			
Ethnicity			33.61	5	< 0.01
White British (WB)	88 (26.51)	131 (43.52)			
White Other (WO)	45 (13.55)	45 (14.95)			
Black African (BA)	83 (25.00)	50 (16.61)			
Black Caribbean (BC)	55 (16.57)	44 (14.62)			
Asian (A)	15 (4.52)	17 (5.65)			
Other (OE)	46 (13.86)	14 (4.65)			
Social class (main)^a			159.40	4	< 0.01
Salariat	31 (10.37)	150 (50.68)			
Intermediate	82 (27.42)	76 (25.68)			
Working class	136 (45.48)	37 (12.50)			
Long term unemployed	26 (8.70)	1 (0.34)			
Student	24 (8.03)	32 (10.81)			
			t	Df	p
Mean age in years (SD)	29 (8.92)	35 (12.34)	7.25	631	< 0.01

^a Missing values: cases = 33 (9.94%), controls = 5 (1.66%). df, degrees of freedom. SD, standard deviation. (Percentages may not add up due to rounding). Figures in bold indicate $p < 0.05$.

4.2 Main effect analyses

This section addressed the study aims 1 and 2, assessing the associations between experience of a) trauma or b) discrimination (independently) and psychosis risk. In addition, exposure to trauma and risk of psychosis is explored by ethnic group.

4.2.1 Lifetime severe traumatic experiences and case-control status

Of the total number recruited into the wider study, 204 cases and 223 controls completed the HTQ. This section addresses the main effect of lifetime trauma on odds of psychosis (Hypothesis 1a).

Cases (65.69%) were more likely to experience one or more severe trauma in their lifetime when compared to controls (37.67%); $\chi^2 = 33.47$, $p < 0.01$; see Table 2 below.

There was evidence to suggest that experience of one or more severe trauma was associated with over three-fold increase odds of psychosis (OR 3.17, 95% CI 2.13 – 4.71, $p < 0.01$). After adjusting for a priori confounders there was a similar increase in odds which remained significant and explained 33% of the variance (adj. OR 3.33, 95% CI 1.97 – 5.63, $p < 0.01$; see Table 3). When looking at the association of trauma and case-control status by ethnicity (exposure and outcome by confounder; using `mhodds` command), although it appeared the OR for association between trauma and status varied by ethnicity (WB OR 2.06, 95% CI 1.02 – 4.16; WO OR 4.97; WO OR 4.97 95% CI 1.32 – 18.65; BA OR 4.31, 95% CI 1.65 – 11.25; BC OR 4.39, 95% CI 1.47 – 13.16; A OR 0.57 95% CI 0.07 – 4.40; OE OR 0.37 95% CI 1.04 – 3.59), this difference was not statistically significant at the conventional level ($\chi^2 = 9.84$, $p = 0.08$), see Table 4. That is, a difference in odds of this magnitude occurs only by chance alone in 8 in 100 analyses. Thus, although odds ratios vary by ethnicity, the evidence was fairly weak as it did not reach conventional threshold.

Table 2. Comparison on severe lifetime trauma experiences between psychosis cases and controls

Variable	Cases (n = 204) n (%)	Controls (n = 223) n (%)	χ^2	Df	p
Severe lifetime trauma ^a			33.47	1	< 0.01
0	70 (33.49)	139 (62.33)			
≥ 1	134 (65.69)	84 (37.67)			

Note. ^a Percentages calculated between cases and controls sample. ^b Percentages calculated within each ethnic group. χ^2 , Chi-Square Test; df, degrees of freedom; ≥, greater than or equal to; #, number; OR, odds ratio; CI, confidence intervals. Figures in bold indicate $p < 0.05$.

Table 3. Association between severe trauma experience and case-control status

Variable	Unadjusted		Adjusted ^a	
	OR (95% CI)	p	OR (95% CI)	p
Severe trauma	3.17 (2.13 – 4.71)	< 0.01	3.33 (1.97 – 5.63)	< 0.01

Note. OR, odds ratio; CI, confidence intervals. Figures in bold indicate $p < 0.01$. ^a Adjusted for age, gender, main social class and ethnicity

Table 4. Association between severe trauma experience and case-control status stratified by ethnicity

Ethnic group	Unadjusted OR	95% CI	p
White British	2.06	1.02 – 4.16	< 0.05
White Other	4.97	1.32 – 18.65	< 0.01
Black African	4.31	1.65 – 11.25	< 0.01
Black Caribbean	4.40	1.47 – 13.16	> 0.05
Asian	0.57	0.07 – 4.40	> 0.05
Other	0.37	0.04 – 3.59	> 0.05
Test of homogeneity of ORs	χ^2	df	p
	9.84	5	> 0.05

Note. χ^2 , Chi-Square Test; df, degrees of freedom; OR, odds ratio; CI, confidence intervals.

4.2.2 Discrimination and risk of psychosis

262 cases and 256 controls completed the discrimination questionnaire. To test the main effect of the number of perceived a) discriminatory events, and b) racial/ethnic vs other reasons for discrimination on odds of psychosis (Hypothesis 1b). The sum of yes/no responses for each discriminatory event were calculated and dichotomised into binary variable (0 or ≥ 1 events). In relation to the main reason for discrimination, the sum of each reason were calculated and then dichotomised to binary variable (discrimination due to race/ethnicity vs other reasons).

4.2.2.1 Number of perceived discriminatory events

Cases (64.50%) were more likely to experience one of more discriminatory events than controls (48.05%); $\chi^2 = 14.26$, $p < 0.01$; see Table 5 below.

There was evidence to suggest that experience of one or more discriminatory events were associated with nearly two-fold increased odds of psychosis (OR 1.96, 95% CI 1.38 – 2.79, $p < 0.01$) and this remained significant even when controlling for *a priori* confounders (adj. OR 1.80, 95% CI 1.15 – 2.84, $p = 0.01$); see Table 6). There was no evidence to suggest that experience of discrimination and case-control status varied by ethnicity ($\chi^2 = 7.64$, $p = 0.18$; see Table 7) as the magnitude of difference in odds occurs only by chance by approximately 2 in 10 times.

Table 5. Basic analyses of discrimination and case-control status

Variable	Cases (n = 262) n (%)	Controls (n = 256) n (%)	χ^2	Df	
Number of discriminatory events^a			14.26	1	< 0.01
0	93 (35.50)	133 (51.95)			
≥ 1	169 (64.50)	123 (48.05)			
Main reason reported			1.88	1	> 0.05
Racial/Ethnicity	190 (72.52)	199 (77.73)			
Other	72 (27.48)	57 (22.27)			

Note. ^a Percentages calculated between cases and controls sample. ^b Percentages calculated within each ethnic group. χ^2 , Chi-Square Test; df, degrees of freedom; ≥, greater than or equal to, #, number. Figures in bold indicate $p < 0.05$.

Table 6. Analyses of discrimination variables and case-control status

Variable	Unadjusted		Adjusted ^a	
	OR (95% CI)	p	OR (95% CI)	p
# of event types	1.96 (1.38 – 2.79)	< 0.01	1.80 (1.15 – 2.84)	= 0.01
Main reason reported	1.32 (0.89 – 1.97)	> 0.05	0.65 (0.38 – 1.12)	> 0.05

Note. #, number; OR, odds ratio; CI, confidence intervals. Figures in bold indicate $p < 0.01$. ^a Adjusted for age, gender, main social class and ethnicity.

Table 7. Association between discrimination and case control status stratified by ethnicity

Variable	Ethnic group	Unadjusted OR	95% CI	p
# of event types	White British	2.08	1.14 – 3.81	< 0.05
	White Other	3.09	1.03 – 9.27	< 0.01
	Black African	0.85	0.39 – 1.87	> 0.05
	Black Caribbean	3.33	1.13 – 9.74	> 0.05
	Asian	0.75	0.10 – 5.77	> 0.05
	Other	0.92	0.23 – 3.75	> 0.05
Test of homogeneity of ORs		χ^2 7.64	df 5	p > 0.05
Main reason racial/ethnicity	White British	2.20	0.73 – 6.69	> 0.05
	White Other	1.56	0.46 – 5.30	> 0.05
	Black African	0.55	0.25 – 1.21	> 0.05
	Black Caribbean	0.87	0.36 – 2.11	> 0.05
	Asian	1.11	0.14 – 9.14	> 0.05
	Other	0.77	0.20 – 2.93	> 0.05
Test of homogeneity of ORs		χ^2 5.03	df 5	p > 0.05

Note. χ^2 , Chi-Square Test; df, degrees of freedom; OR, odds ratio; CI, confidence intervals.

4.2.2.2 Racial discrimination vs other reasons

There were no significant differences between cases (27.48%) and controls (22.27%) in relation to reporting whether participants perceived their discriminatory experiences were due to racism/ethnic discrimination or other reasons ($\chi^2 = 1.88$, $p > 0.05$; see Table 5). Logistic regression analysis did not show any evidence to support that perceived racism/ethnic discrimination increased odds of psychosis (see Table 6 above). In addition, there was no evidence to show that reasons of discrimination and case-control status varied by ethnicity ($\chi^2 = 5.03$, $p > 0.05$; see Table 7).

4.3 HTQ and BCSS

192 cases and 214 controls were assessed with HTQ and BCSS for the relevant analyses in this section.

4.3.1 Mediation analyses

Analyses were conducted to test whether negative views of a) oneself and b) others lie on pathway (i.e. the mediating effect) between exposure to severe trauma and development of psychosis (Hypothesis 3).

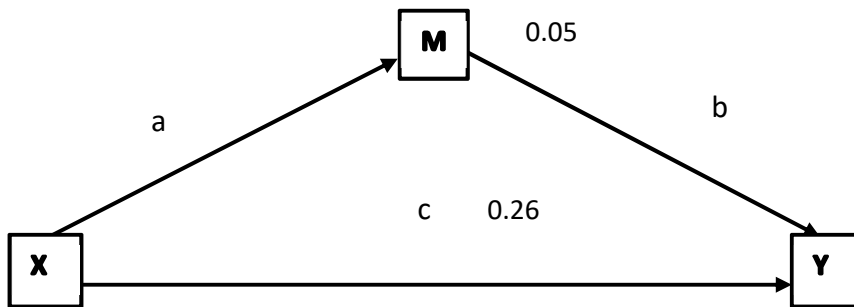
The total, direct and indirect effects of severe trauma and core beliefs about a) self or b) others are presented in Table 8. Negative beliefs about oneself mediated approximately 15% of the total effect which suggest only a small proportion of the effect of trauma on psychosis was via beliefs about self. Negative beliefs about others mediated approximately 11% of the total effect, again which suggest only a small proportion of the effect of trauma on psychosis was via beliefs about others. The trauma and case-control associations were only marginally mediated by either the presence of negative beliefs about oneself or others in this sample, suggesting that other factors may also be likely to be involved in these pathways.

Table 8. Total, direct and indirect effects of severe trauma and negative core beliefs on case-control status

	Pathway	Unadjusted standardised coefficient (95% CI) ^a	% of effect mediated by schematic belief
Trauma & negative beliefs of self	Direct effect	0.26 (0.14 – 0.35)	15.31
	Indirect effect	0.05 (0.18 – 0.08)	
	Total effect	0.30 (0.18 – 0.40)	
Trauma and negative beliefs of other	Direct effect	0.28 (0.16 – 0.38)	10.52
	Indirect effect	0.32 (0.05 – 0.06)	
	Total effect	0.31 (0.19 – 0.41)	

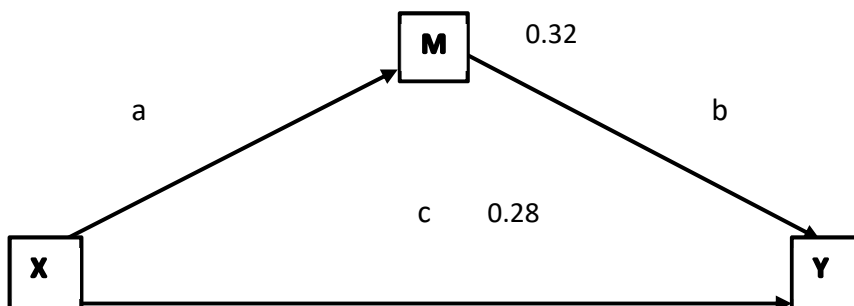
Note. CI, confidence interval; ^a bias corrected.

(a) Negative beliefs about oneself

*Figure 3. Diagram of mediating effect of negative beliefs of oneself.*

Note: X = severe lifetime trauma; Y = Odds of psychosis; M = negative beliefs of oneself

(b) Negative beliefs of others

*Figure 4. Diagram of mediating effect of negative beliefs of others.*

Note: X = severe lifetime trauma; Y = Odds of psychosis; M = negative beliefs of others

4.3.2 Moderation analyses

To examine whether exposure to trauma combined with presence of negative schematic beliefs of a) oneself and b) others to increase odds of psychosis beyond the effects of each alone (Hypothesis 4).

There was no evidence that negative beliefs about oneself modified the association between trauma and odds of psychosis (0.93, 95% CI 0.44 – 1.94), see Table 9. That is, the odds ratio does not differ by more than chance across the Strata, the effect of trauma on psychosis is similar in

those with negative beliefs of oneself (OR = 3.40; 95% CI 1.90 – 6.09; $p < 0.01$) and those without such beliefs (OR = 2.17; 95% CI 1.19 – 3.95). Thus, the results indicated that presence of negative beliefs of oneself did not substantially alter the associations (Irttest $\chi^2 = 1.11$, $p > 0.05$). In contrast, there was evidence that the impact of traumatic events depended on appraisals in relation to beliefs about others. The odds of psychosis significantly differed across the strata, such that the effect of trauma on psychosis was greater in those with negative beliefs of others (OR = 5.24; 95% CI 3.09 – 8.88; $p < 0.01$) than in those without such beliefs (OR = 0.93; 95% CI 0.45 – 1.94; $p > 0.05$). This interaction was significant at the p-level of 1% (Irttest $\chi^2 = 14.25$, $p < 0.01$).

Table 9. Negative schema test of modification on association between trauma and case-control status

Negative schema	Unadjusted OR	95% CI	P	χ^2	df	p
Self						
Absent						
Present	1.57	0.68 -3.61	> 0.05	1.11	1	> 0.05
Others						
Absent						
Present	5.64	2.28 – 13.95	< 0.01	14.25	1	< 0.01

5. Discussion

5.1 Summary of findings

The findings of this study provided evidence that increased prevalence of severe lifetime trauma was associated with over three-fold increased odds of psychosis. There were also weak (but suggestive) evidence to support the mediation of both negative beliefs of oneself (15%) or others (11%). Negative beliefs of oneself or others, only partially mediated the association between exposure to trauma and odds of psychosis. In addition, negative beliefs of others but

not of oneself moderated this effect of trauma on the odds of psychosis. As hypothesised, the odds of psychosis were highest in those exposed to severe trauma who had negative beliefs about others. There was no support that negative core beliefs of oneself modified the association between trauma and case-control status. In relation to the experience of discrimination, the number of events experienced but not the perceived reason for the discrimination was supported with evidence that this increased the odds of psychosis. For the main effects of trauma and discrimination on risk of psychosis, there was no evidence that exposure to these events varied significantly by ethnicity than would be expected by chance alone.

5.2 Methodological considerations

Although some findings presented are consistent with previous research, a number of methodological issues need to be considered when interpreting the findings. Many of these limitations are related to the disadvantages of using cross-sectional case-control design and reliance on retrospective self-report. One key reason is that reports of adverse experiences may be confounded by psychopathology (2011); thus may produce unreliable and inaccurate accounts of events. Nevertheless, some research has provided evidence which may weaken these arguments. Fisher and colleagues (2011) provided evidence for the reliability of reports of adverse events are not necessarily confounded by psychopathology. They go on to suggest that discrepancies in such reports from individuals' documented notes are largely due to failure by clinicians to enquire about abusive experiences (John Read & Fraser, 1998; John Read, McGregor, Coggan, & Thomas, 2006; Rose, Peabody, & Stratigeas, 1991). Moreover, individuals are more likely to underreport abuse than to make false or exaggerated claims (John Read, 1997). In the study, steps were made to ensure individuals were treated sensitively and the majority would have been visited multiple times by researchers, thus reducing possibilities of information bias. In addition, the majority of assessments were conducted as semi-structured

interviews allowing the researchers to explore ambiguous answers and any remaining queries were discussed by the research team before reaching a consensus.

The case-control design employed by this study may also introduce other challenges such as selection bias and reverse causality. Selection bias refers to the methodology used to select cases and controls from the population which confounds the effect of exposure on outcome. There are a number of ways this may have occurred in relation to methodology used in this study. Cases and controls were assigned to independent groups in which the presence or absence of disorder was seen as the most important condition. This is problematic as selection on the basis of case or control status may be in some way linked to the exposure or outcome under observation (in this case experience of trauma). Thus, this may lead to an overestimation of exposure to trauma in cases or underestimation in controls, thereby inflating the magnitude of the associations found between trauma and odds of psychosis. Selection bias may have also arisen from characteristics of subjects who are more likely to take part in the study. In any case, the controls in the study was representative of the sample population in the area, and a rigorous sampling method was employed. Though it is important to note that selection bias cannot be completely removed. In relation to reverse causality, it is difficult to rule out in cross-sectional studies if the presence of illness or disorder enhanced the probability of the exposure to occur, i.e. the disorder caused the exposure and not the other way around. In addition, the inclusion of eliciting events throughout the lifetime, as was the case for the measurement of trauma and discrimination in this study, makes it difficult to distinguish whether outcomes (i.e. disorder) arose due to exposure or vice versa. The alternative approach which may handle such an issue would be to conduct prospective longitudinal studies, which is difficult not least because psychosis is a rare disorder but also such studies are likely to be costly and unfeasible (Moffitt, Caspi, & Rutter, 2005).

As with many epidemiological studies, sample size is often an issue. This is even more amplified when studies seek to extract information relating to ethnic differences or uncover explanatory mechanisms. Specifically, as this may reduce sample size even further or samples may not be representative enough to generalise findings. This is not likely to be an issue for the main effects as the post-hoc power analysis revealed that the study had over 95% power to detect any differences. However, this may have been an issue in analyses that stratified samples by ethnicity or sought to explore mediating or moderating effects of schemas. The additions of these variable reduce the sample size within the analyses thus may reduce power to detect differences if present. This issue may add to the difficulty of interpreting the results with relation to magnitude of effect of ethnicity on the associations and in the analyses of the possible pathways between the relations of trauma and psychosis risk.

Finally, the present study did not include any measures of genetic risk and other important environmental exposures such as drug use and migration (although this data was available in the wider study). It is important to note that these factors may have contributed to the onset and development of psychosis as emphasised in previous literature. Indeed, as highlighted in the introduction the aetiology of psychosis is multifaceted and likely to include a whole range of complex biopsychosocial processes and mechanisms. In addition, adverse events have been shown to cluster within individuals and accumulate over time (Johnsson, Zolkowska, & McNeil, 2015), with evidence of a dose-response relationship in increasing risk of psychosis (Fisher et al., 2011; Kelleher et al., 2013; Larkin & Read, 2008); (Shevlin, Houston, Dorahy, & Adamson, 2007). Thus, the possibility of the confounding influence of these factors which may be independent of, mediate or moderate the associations found in this study cannot be ruled out. Nevertheless, the approach utilised in this study precludes us from inferring causality (Morrison et al., 2003). Nonetheless, the study recruited a relatively large sample and employed several approaches which surpass methodological limitations of previous studies (see for review: (Morgan & Fisher,

2007). Specifically, this study sought to assess trauma and discrimination ensuring that the nature, severity, timing and information pertaining to duration were collected from individuals. In addition, when assessments of trauma were unclear, ambiguities were clarified by consensus. The study also has strengths in its robust approach to ensuring selection of representative and ethnically diverse sample.

5.3 Considerations of the findings

These limitations notwithstanding, this study highlighted important findings which are in line with previous literature. One of the key findings revealed in this study was that the exposure to adverse stressors such as trauma and discrimination increased the odds of psychosis. This finding is consistent with previous studies which demonstrated that adverse experiences are a risk factor for psychosis (see reviews; Matheson et al., 2013; Varese et al., 2012). Furthermore, these relationships were found to be robust even when controlling for possible sociodemographic confounders (e.g. age, gender, ethnicity, main social class). However, there was no indication that some groups were more at risk, for example by ethnicity. The evidence is suggestive that trauma and discrimination are negative experiences which can have detrimental effects on mental health outcomes irrespective of ethnicity. Although, it is important to note with respect to how this applied to the relationship between trauma and psychosis risk that this finding should be interpreted with caution. As the significance level ($p = 0.08$) only narrowly fell short of conventional p -value < 0.05 , it may be that the sample size was underpowered to detect any difference. With respect to discriminatory events, there was no evidence to suggest that the perception of racism or ethnic discrimination increased the odds of psychosis. Of note however, the prevalence of discrimination experienced by cases (64.50%) and controls (48.05%) were higher than estimates found in some studies, for example, Kessler and colleagues (Kessler et al., 1999) found only a prevalence of 33.50% in their sample.

In relation to explanatory models of psychosis, core schemas have been identified as a possible mechanism which explains the impact of exposure to trauma on psychosis risk (Garety et al., 2001). This study found weak evidence that the presence of either negative schematic beliefs about oneself or others, to a small extent, partially mediated the effect of exposure to one or more traumatic events to increase odds of psychosis. However, due to the methodology employed by this study it is difficult to measure the temporal relationship between exposure to trauma and the development of core beliefs. This is an important issue as the experience of trauma may lead to the development negative core schemas (Garety et al., 2001). However, reverse causality may also be possible as the presence of negative beliefs may predispose an individual to the negative effects of experiencing trauma. Interestingly, this study did find evidence for the moderating effects of trauma and negative core beliefs about others (but not oneself) on psychosis risk. That is, the experience of one or more severe lifetime trauma and the presence of negative beliefs about others, increased the odds of psychosis beyond the effects of each alone. This is in line with Garety and colleagues (2001) cognitive model of psychosis, as it suggests that the experience of trauma may re-activate negative schemas about others, and it is this reactivation of latent beliefs which increase the risk of developing a psychotic disorder. As highlighted above psychosis may arise through a search for meaning, and a negative experience like trauma may activate underlying vulnerabilities which lead to biased appraisals that manifest as psychotic symptoms (Hardy, 2017).

5.4 Implications for clinical psychology

The present findings have important implications for the course and treatment of psychosis. The findings highlighted that adverse experiences such as of trauma and discrimination are potentially implicated in amplifying the risk of psychosis. These observations are important in terms of understanding the nature of the relationship between adverse experiences and has

significant clinical implications. The experience of trauma and discrimination may likely complicate the clinical presentation of psychosis and be associated with great complex needs. However, experiences such as trauma are often underreported or under-recognised. Despite the elevated rates of trauma in psychosis, clinicians do not routinely ask patients about traumatic experiences (Cunningham et al., 2016). This is in spite of evidence suggesting that trauma can have long-lasting and detrimental effects on an individual's psychosocial wellbeing by impacting on other variables such as cognitive and affective processes (see Aas et al., 2011; Garety et al., 2007; Garety et al., 2001; Kilcommons & Morrison, 2005)). Psychotic symptoms may be interconnected with interpretations of the social context, thus making social experiences important (Bebbington, Fowler, Garety, Freeman, & Kuipers, 2008). Therefore, findings from the study lends support in completing comprehensive assessment which will elicit these kinds of experience as they are likely to provide important context of an individual's history and current social world (Fowler, 2000).

The results also point to the need of providing support and interventions to individuals after such experiences, taking into account the underlying meaning of such events. As trauma and negative beliefs about others increased odds of psychosis, these associations reveal something about which individuals are most likely to be at risk and can enable us to ask key questions. Therefore, this finding provides support for the use of trauma-focused Cognitive Behavioural Therapy (tf-CBT) in psychosis. Indeed, several research papers have found beneficial effects of tf-CBT in psychosis populations with experience of trauma (Hardy, Smith, Gottlieb, Mueser, & Steel, 2013; Smith et al., 2007). In addition, the principles from Compassion Focused Therapy (CFT; Gilbert, 2010) which promote the development and enhancement of compassion for oneself and others may help reduce negative schemas of individuals with psychosis. Studies of CFT have shown some promise in their application to psychosis. Mayhew and Gilbert (2008), found reductions in persecution and malevolence in individuals who hear malevolent voices.

Although schemas are considered to be relatively stable, psychological interventions may help to normalise an individuals' experiences, foster development of a more accepting stance towards their core beliefs, and place emphasis on generating alternative and more helpful explanations for distressing beliefs and experiences (Gamble & Brennan, 2005; Oliver, O'Connor, Jose, McLachlan, & Peters, 2012). An individual's distress and symptom-maintaining beliefs may be best understood in the context of stressful experiences such as trauma, its meaning and the degree to which the events have remained unresolved e.g. (Andrew, Gray, & Snowden, 2008).

Nevertheless, it is sensible not to overstate the potential benefits of the insights this study provides in terms of applications to psychological interventions. The experience of trauma is common, and unlikely to be preventable, therefore unamenable to change given that there is no guarantee to prevent or control the vase climate of human experiences. In addition, what constitutes a trauma experience is subjective which can and does vary from one individual to the other and even within the same individual in different contexts. However, such assertions should not preclude the application of insights found in this study which may lead to potential targets for future research and therapeutic advancements that promote and enhance psychological wellbeing. Understanding the population characteristics and risk factors for psychosis could lead to faster or better assessment and/or effect treatments for those individuals at great risk. In identifying the potential mechanisms which put one groups more at risk than others, this study serves as an important step in enhancing knowledge in this area. It potentially captures a significant population given the huge burden psychosis can place on individuals (Murray, 2012; Van Os & Kapur, 2009).

5.5 Conclusion

Despite the expansive research in this area and the findings from this study, it is difficult to establish cause and effect relationships in the associations found. Inevitably, there are a number of ways in which trauma events and its consequences can differ considerably not only between individuals, but within the same individual across different contexts. Moreover, it is important to state that this study is not suggesting that exposure to experiences of trauma or discrimination are either necessary or sufficient for the development of psychosis. There are likely to be multiple biopsychosocial factors involved and not all individuals exposed to trauma go on to develop a psychotic disorder. An important take home message, though, is that the experiences of adverse experiences such as trauma and discrimination are important to consider in relation to risk of psychosis. The study also highlighted that although the rates of traumatic experiences differ within ethnic groups, these differences were not sufficient to explain the relationship between trauma and psychosis. However, when individuals held negative beliefs about others and were exposed to trauma, the combination of these effects increased odds of psychosis. These associations are by no means comprehensive. Factors of interest were investigated by the study in which the scope of the analysis were constrained within the timeframe of a doctoral thesis. Further research on the prevalence of adverse experiences, and other factors associated with psychosis may provide more insight on understanding these associations.

6. References

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7. Appendix

7.1 Participant information sheet and Consent form Information and Consent Form (not for data entry)

You have been asked to take part in a study being conducted in the South London and Maudsley NHS Trust. Before you decide whether to enter the study, it is important that you understand why the research is being done and what it will involve. Please take time to read the following information and ask any questions if something is not clear or you wish to know more.

TITLE OF PROJECT: GENETICS AND PSYCHIATRIC ILLNESS (GAP)

What are the aims of the study?

In our research project we are interested in identifying what the main risk factors that predispose to psychosis are. In particular, we want to know whether there are any genes that increase the risk of developing a psychotic disorder, either alone or by interacting with environmental factors such as stress, cannabis, and infections. Part of the reason why some people become ill may lay in genetic differences between people, in the same way that we are different in the colour of our eyes, hair etc. To achieve this, we will compare the genetic make-up of people with a diagnosis of psychosis with the make-up of people with similar characteristics but no history of mental health problems.

We also aim to establish whether some genes might influence the course of the illness and response to medication. Some patients experience an improvement of their psychiatric symptoms when they are treated with medications, whereas others do not do so well and/or experience severe side-effects. Therefore we aim to look at how genes can influence individual differences in response to drug treatment so that we may be able to choose better drugs for each person. The type of genetic analysis that we carry out is only for research purposes and does not at present produce clinically relevant results.

Finally, an additional aim of the study is to understand how the social environment may contribute to the onset of illness and the illness experience.

Why are we asking for your help?

You have been invited to take part in this study because of the nature of the symptoms that you appear to have been experiencing. During the course of the study approximately 1000 people who have had symptoms like yours will be asked to take part.

Note that a patient does not have to be involved in the GAP project research and, if they decide not to take part, it will not affect their current or future medical care in any way.

What will we ask of you if you take part in the study?

For this project we will ask from you a small sample of blood, about 20 mL (a few tablespoons full) or cheek swab and saliva samples for metabolic and genetic analysis. We may also use your blood and saliva sample to:

- 1) Measure the level of hormones and proteins contained in the blood serum and in the saliva.
- 2) Look at the expression of some genes of interest in the white cells contained in the blood.

A medically trained researcher will take the blood sample using disposable sterile equipment. It will only take few minutes as for any routine blood sample. If you are unable or unwilling to give a blood sample it is also possible to perform genetic analysis from cheek swab samples, a simple procedure

that (we can show you the kit and illustrate the procedure) collects dead cells present in your saliva and in your mouth. From the cheek swab sample we cannot measure level of medication or look at expression of genes, we can only extract a small amount of DNA. Therefore we prefer to ask for a blood sample to guarantee a better quality of our results and make the most out of your generous help.

A researcher will demonstrate how to collect the saliva sample and will provide you with the tubes required. The level of some proteins contained in the saliva can give us an indication of differences in the level of stress experienced by healthy volunteers and people suffering from mental illnesses.

We will also ask for some of your time to collect clinical and socio-demographic information using standardised research instruments: diagnostic interview, symptoms rating scale, socio-demographic interview and neuropsychological tests. We may also ask you to participate in an interview asking about your own perspectives on your social environment and your health condition.

If you have already taken part in other research projects at the Institute of Psychiatry, London that involved some of the assessment we are interested in, we will not ask you to undergo them again but we request your permission to use the existing data.

Some people within the study will be invited to undergo an MRI scan of the head and of another region of the body (the adrenal gland, a small gland above the kidney). They will be presented with separate information and consent forms for this procedure.

The sample collection and the clinical assessment will require approximately 3 hours of your time. Moreover we would like to contact you again for follow up (up to 24 months) to repeat the above assessments to investigate changes over time. We will also reimburse any travel expense related to your participation into the study.

We will also ask for your consent to contact your GP, mother (or father) and a sibling. This is 1) to collect information from your GP records and mother about events that may have occurred very early in your life, such as complications during pregnancy and neonatal infections, 2) to conduct some of the same assessments with your sibling that we have conducted with you, and 3) to ask your sibling similar questions that we have asked you about the environment in which you both grew up and experiences you may have had in childhood. We will only contact your GP and/or relative(s) with your explicit consent and we will not disclose any information we have collected from you to them. If you agree for us to contact your mother (or father) and/or a sibling, we will only proceed to interview them if they provide consent.

What are the risks?

The risks involved are those of ordinary blood tests such as small pain and occasionally a small bruise around the area from where the sample has been taken. There is no risk involved in the collection of saliva.

Is Confidentiality guaranteed?

All personal information about you is regarded as strictly confidential; only researchers belonging to the study team, and not external collaborators, know which sample belongs to whom. All the information about you will be coded; you will not be identifiable in any research outcome.

1) The blood samples first and the DNA samples after extraction will be stored in the Institute of Psychiatry secured laboratory until reporting is complete.

2) The samples will be coded using bar codes (numbers and letters not referring to your name or date of birth) that will be entered on a secure computerized data base.

3) The clinical information collected on the sample will be securely held in the Institute of Psychiatry building.

4) Nothing that you have told us will be mentioned to any relative you might give us permission to contact.

The access to the samples and the related information will be restricted to the researchers involved in the study. In case of commercial collaborations only the coded data will be shared, therefore no researcher external to the study team will ever have access to personal data concerning participants.

Any future work will pursue aims related to the topic of this project and any extension of the project beyond 5 years, will be subject to review by a research ethics committee. You are free to withdraw from this study at any point without giving a reason by contacting the researcher whose details are at bottom of the consent form. Withdrawal will not affect any of the care and treatment you receive.

What are the benefits for you of taking part?

This is a research project, looking at comparing a group of healthy volunteers with people experiencing their first psychotic episode. As mentioned before, this study will not produce individual test results for any of the data collected. Therefore we cannot offer direct benefits for you. We will be able to provide all participants with a general summary of our research, when the project is complete, through a project newsletter. Our research study is also described on the Institute of Psychiatry general website (www.iop.kcl.ac.uk), under the Department of Psychosis Studies section.

Who is funding this project?

This study is funded by the The Maudsley Charitable Fund, the Department of Health, the Wellcome Trust and the European Union. Thank you very much for your time and once again please ask for more information on both the project and/or your illness/symptoms if it is still unclear.

Contact details for research team:

Dr Marta Di Forti

Institute of Psychiatry

Tel 020 7848 5352

e-mail: marta.diforti@kcl.ac.uk

CONSENT FORM

If you have come to the decision to enter the study after carefully considering the information provided, please read and sign this form.

TITLE OF PROJECT: GENETICS AND PSYCHIATRIC ILLNESS (GAP)

Researcher: Dr Marta Di Forti, Institute of Psychiatry

- | | | |
|---|---------------------------------|--------------------------------|
| 1) I have read the information sheet and I have been given a copy. I was given the opportunity to ask questions. I understand why the research is being done and the risks involved. | Yes
<input type="checkbox"/> | No
<input type="checkbox"/> |
| 2) I agree to give a sample of blood/cheek swab and saliva samples for research in the above project. I understand how the sample will be collected, that giving the sample is voluntary and that I am free to withdraw at any time without giving a reason, and without my medical treatment or legal rights being affected. I understand that I will be contacted in the future to repeat part of the assessment. | Yes
<input type="checkbox"/> | No
<input type="checkbox"/> |
| 3) I understand that research using the sample I give will involve genetic analysis aimed at understanding the role of genes in disease and response to drugs, that the data produced are for research rather than clinical purposes, and that these results will have no implications for me personally. | Yes
<input type="checkbox"/> | No
<input type="checkbox"/> |
| 4) I understand I will not receive any 'test' results from this study, because the assessment I will undergo, does not produce clinically relevant information but just research data. The project newsletter will describe the general importance of any research results obtained. | Yes
<input type="checkbox"/> | No
<input type="checkbox"/> |
| 5) I give permission for my previous research records to be looked at, and information from them to be analysed in strict confidence by responsible professional staff from the research team. Researchers external to the study team, collaborating in the project (including commercial collaborations) will only access my coded data. | Yes
<input type="checkbox"/> | No
<input type="checkbox"/> |
| 6) I agree that the samples I have given and the information gathered about me can be examined and stored until reporting is complete at the Institute of Psychiatry. I understand that future authorised research may be performed by researchers other than those who conducted the first project, including researchers from commercial organisations. To guarantee confidentiality, I agree that researchers external to the study team, including those from commercial collaborators, will only have access to coded data and not to personal details. Any future research will only pursue aims related to the topic of this project, and any extension of the project will be subjected to review by a research ethics committee. | Yes
<input type="checkbox"/> | No
<input type="checkbox"/> |
| 7) I consent to the input of coded data obtained from my blood sample and from the information gathered about me into a computer, to be used for statistical analysis and research. I understand I have the right to request, via the study co-ordinator, to review data concerning me, and to have such data modified if inaccurate, or deleted. | Yes
<input type="checkbox"/> | No
<input type="checkbox"/> |
| 8) I consent to participate in a digitally-recorded interview about my own perspectives on my health condition and on my social experiences. I understand that this interview would be recorded to ensure that my own views are adequately represented. | Yes
<input type="checkbox"/> | No
<input type="checkbox"/> |
| 9) I understand I will not benefit financially if this research leads to the development of a new treatment of medical test but my travel expenses will be reimbursed. | Yes
<input type="checkbox"/> | No
<input type="checkbox"/> |
| 10) I give permission for my GP records to be looked at. | Yes
<input type="checkbox"/> | No
<input type="checkbox"/> |

11) I agree to my mother being approached to participate in this study.

Yes
☐

No
☐

Contact details:

Name

Address

Phone Number

12) I agree to a sibling being approached to participate in this study.

Yes
☐

No
☐

Contact details:

Name

Address

Phone Number

.....
Name of Subject	Date	Signature
.....
Name of Researcher	Date	Signature

Would you like to be sent further information about the project in our newsletter?

Yes
☐

No
☐

Contact details for research team:

Dr Marta Di Forti

Institute of Psychiatry

Tel 020 7848 5352

e-mail: marta.diforti@kcl.ac.uk

7.2 Measures used in the study

Schedules for the Assessment of Social Contexts and Experiences

Subject number: 2EU02. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	Date of Birth <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 1 <input type="text"/> 9 <input type="text"/> <input type="text"/> <input type="text"/>
Date <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 2 <input type="text"/> 0 <input type="text"/> <input type="text"/> <input type="text"/>	

SCHEDULES

COMPLETED

MRC Sociodemographic Schedule (Amended) (Pt. 1)

Yes ☐₁

No ☐₂

MRC Sociodemographic Schedule (Amended) (Pt. 2)

Yes ☐₁

No ☐₂

List of Threatening Experiences (I) (+HTQ)

Yes ☐₁

No ☐₂

Childhood Experiences of Care and Abuse (I)

Yes ☐₁

No ☐₂

Bullying

Yes ☐₁

No ☐₂

Discrimination

Yes ☐₁

No ☐₂

Brief Impact of Events Scale

Yes ☐₁

No ☐₂

Social Environment Assessment Tool

Yes ☐₁

No ☐₂

Significant Others

Yes ☐₁

No ☐₂

Harvard Trauma Questionnaire

PART I

Below is a list of events you may have encountered at some point during your life. For each event please tick all that apply:

Event	Experienced	Witnessed	Heard about it	No
Combat situation				
Lack of food or water				
Lack of shelter				
Being close to death				
Illness without access to medical care				
Forced separation from family members				
Unnatural death of family/friend				
Lost or kidnapped				
Torture				
Murder of family/friend				
Serious injury				
Imprisonment				
Murder of strangers				
Sexual abuse or rape				
Brainwashing				
Forced isolation from others				
Other situation that was very frightening				

PART II

Please describe the most traumatic event(s) you have experienced:

Discrimination

Time interval: Lifetime

Interviewer:

Date

____-____-20____

In the following questions we are interested in the way other people have treated you or your beliefs about how other people have treated you. Can you tell me if any of the following has ever happened to you? Please indicate number of times, age at first occurrence and note the main reason for this. Then:

For any reason, have you ever been unfairly...

	Yes	No	No. of times	Age (first occurred)
1. Fired	O1	O0	<div style="border: 1px solid black; width: 30px; height: 20px; display: inline-block;"></div>	<div style="border: 1px solid black; width: 30px; height: 20px; display: inline-block;"></div>
Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):				
2. Not hired for a job	O1	O0	<div style="border: 1px solid black; width: 30px; height: 20px; display: inline-block;"></div>	<div style="border: 1px solid black; width: 30px; height: 20px; display: inline-block;"></div>
Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):				
3. Denied promotion	O1	O0	<div style="border: 1px solid black; width: 30px; height: 20px; display: inline-block;"></div>	<div style="border: 1px solid black; width: 30px; height: 20px; display: inline-block;"></div>
Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):				
4. Stopped, questioned threatened by police	O1	O0	<div style="border: 1px solid black; width: 30px; height: 20px; display: inline-block;"></div>	<div style="border: 1px solid black; width: 30px; height: 20px; display: inline-block;"></div>
Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):				
5. Treated by court system	O1	O0	<div style="border: 1px solid black; width: 30px; height: 20px; display: inline-block;"></div>	<div style="border: 1px solid black; width: 30px; height: 20px; display: inline-block;"></div>
Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):				

For any reason, have you ever been unfairly...

	Yes O1	No O0	No. of times <div><div></div><div></div></div>	Age <div><div></div><div></div></div>
6. Discouraged from continuing education				

Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):

	Yes O1	No O0	No. of times <div><div></div><div></div></div>	Age <div><div></div><div></div></div>
7. Prevented from buying, renting flat or house				

Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):

	Yes O1	No O0	No. of times <div><div></div><div></div></div>	Age <div><div></div><div></div></div>
8. Treated by neighbours or your family				

Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):

	Yes O1	No O0	No. of times <div><div></div><div></div></div>	Age <div><div></div><div></div></div>
9. Denied a loan or preferable mortgage rate				

Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):

	Yes O1	No O0	No. of times <div><div></div><div></div></div>	Age <div><div></div><div></div></div>
10. Received worse service than other people				

Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):

	Yes O1	No O0	No. of times <div><div></div><div></div></div>	Age <div><div></div><div></div></div>
11. Treated when getting medical care				

Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):

	Yes O1	No O0	No. of times <div><div></div><div></div></div>	Age <div><div></div><div></div></div>
12. Treated when using public transport				

Reason O1 Gender O2 Race, ethnicity O3 Religion O4 Mental Illness O5 Sexuality O6 Age O7 Other (specify):

The Brief Score Schema Scales

Subject number: 2EU02. 	Date of Birth 1 9
Time interval: Present	
Interviewer:	Date 2 0

This questionnaire lists beliefs that people can hold about themselves and other people. Please indicate whether you hold each belief (NO or YES). If you hold the belief then please indicate how strongly you hold it by circling a number (1-4). Try to judge the beliefs on how you have generally, over time, viewed yourself and others. Do not spend too long on each belief. There are no right or wrong answers and the first response to each belief is often the most accurate.

MYSELF	NO	YES	Believe it slightly	Believe it moderately	Believe it very much	Believe it totally
1. I am unloved	O0	O1	O1	O2	O3	O4
2. I am worthless	O0	O1	O1	O2	O3	O4
3. I am weak	O0	O1	O1	O2	O3	O4
4. I am vulnerable	O0	O1	O1	O2	O3	O4
5. I am bad	O0	O1	O1	O2	O3	O4
6. I am a failure	O0	O1	O1	O2	O3	O4
7. I am respected	O0	O1	O1	O2	O3	O4
8. I am valuable	O0	O1	O1	O2	O3	O4
9. I am talented	O0	O1	O1	O2	O3	O4
10. I am successful	O0	O1	O1	O2	O3	O4
11. I am good	O0	O1	O1	O2	O3	O4
12. I am interesting	O0	O1	O1	O2	O3	O4
OTHER PEOPLE	NO	YES	Believe it slightly	Believe it moderately	Believe it very much	Believe it totally
1. Other people are hostile	O0	O1	O1	O2	O3	O4
2. Other people are harsh	O0	O1	O1	O2	O3	O4
3. Other people are unforgiving	O0	O1	O1	O2	O3	O4
4. Other people are bad	O0	O1	O1	O2	O3	O4
5. Other people are devious	O0	O1	O1	O2	O3	O4
6. Other people are nasty	O0	O1	O1	O2	O3	O4
7. Other people are fair	O0	O1	O1	O2	O3	O4
8. Other people are good	O0	O1	O1	O2	O3	O4
9. Other people are trustworthy	O0	O1	O1	O2	O3	O4
10. Other people are accepting	O0	O1	O1	O2	O3	O4
11. Other people are supportive	O0	O1	O1	O2	O3	O4
12. Other people are truthful	O0	O1	O1	O2	O3	O4

7.3 Data preparation and preliminary analyses

All analyses were conducted using Stata Version 14 (Stata, 2015). Analysis commenced with data cleaning and normality assessment for each of the continuous variable of interest in this study (i.e. for trauma, discrimination and core schema variables) by inspecting histograms, basic demographics such as means and medians and assessing skewness and kurtosis.

From examining the normality of the variables of interest in this study, all of the data displayed non-normal distribution (see Table 10. below for statistical summary descriptive of all variables including skewness and Kurtosis). Therefore, to examine the relationships between exposure and outcomes including mediator and moderators, data for trauma, discrimination and core schemas were recoded into binary variables. To dichotomise the scores for trauma and discrimination, the total number of event were summed up and categorised into 0 or 1 or more types of events. For the schema variables, total scores for belief about self or others were dichotomised to 0 vs 1 or more.

Table 10. Basic statistical information for variables of interest including skewness and Kurtosis.

Variable	Descriptive	Median	Mean	Std. dev	Skewness	Kurtosis
sorted by:						
Trauma	Total sample	1	1.26	1.97	2.64	12.08
	Cases	1	2.02	2.45	1.88	7.32
	Controls	0	0.57	0.97	3.13	19.33
Discrimination	Total sample	1	1.40	1.82	1.66	5.69
	Cases	1	1.82	2.03	1.29	4.32
	Controls	0	0.97	1.45	2.14	8.20
Negative self schema	Total sample	1	2.38	3.84	2.25	8.52
	Cases	2	3.81	4.72	1.52	4.92
	Controls	0	1.18	2.28	3.16	17.64
Negative other schema	Total sample	3	5.47	6.30	1.20	3.63
	Cases	6	7.40	6.90	0.78	2.52
	Controls	2	3.84	5.22	1.68	5.76

Note. Std. Dev = standard deviation.

It is acknowledged that using dichotomous variables may lead to a reduction of the study's statistical power (DeCoster, Iselin, & Gallucci, 2009; MacCallum, Zhang, Preacher, & Rucker, 2002). However, using this approach is in line with previous literature in this area examining cognitive pathways between adverse experiences and odds of psychosis (Fisher et al., 2012). Furthermore, dichotomisation is assumed to work better when variables are highly skewed, and can be beneficial for potential non-linear relationships between variables and outcomes

(Farrington & Loeber, 2000). Another important consideration when using dichotomous variables, is whether the measures used have high reliability (De Coster, Gallucci, & Iselin, 2011; DeCoster et al., 2009), and this is observed in the current study as the measures assessing core schemas are said to be stable across time and have good psychometric properties (Fowler et al., 2006). In addition, categorising variables has been suggested to improve communication of research outcomes by making findings easier to interpret and understand (Farrington & Loeber, 2000). Therefore, given the skewed nature of the data, the non-linear relationship between the variables and outcome and above arguments, this approach appears to be justified.